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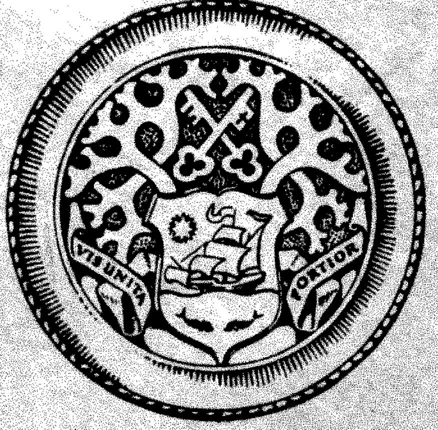

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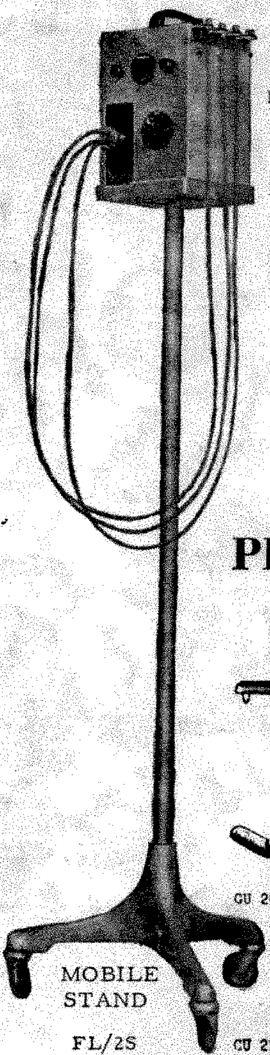

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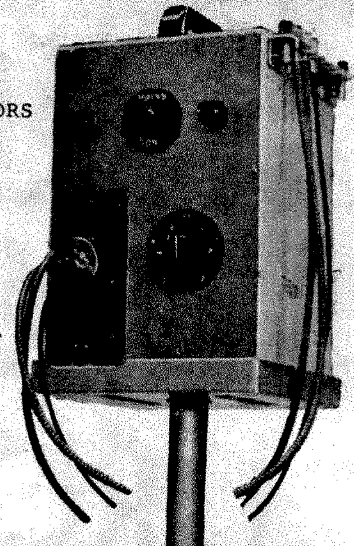

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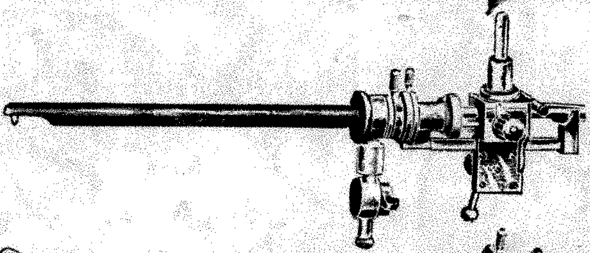

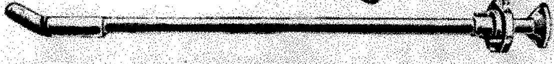

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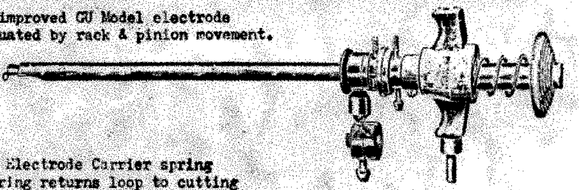

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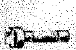

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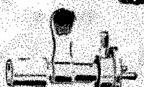

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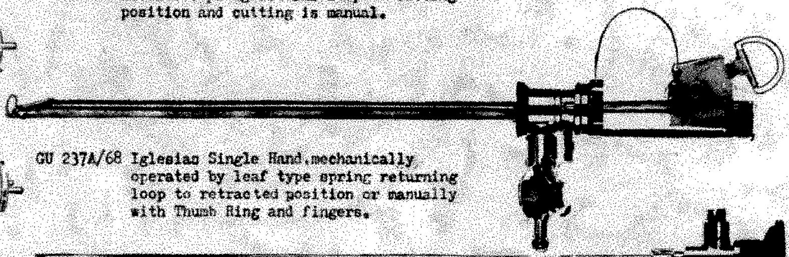

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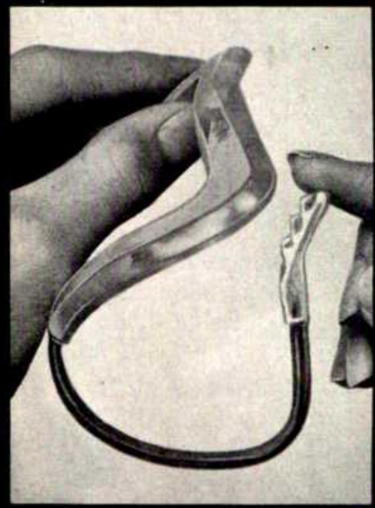

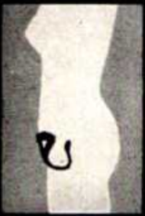

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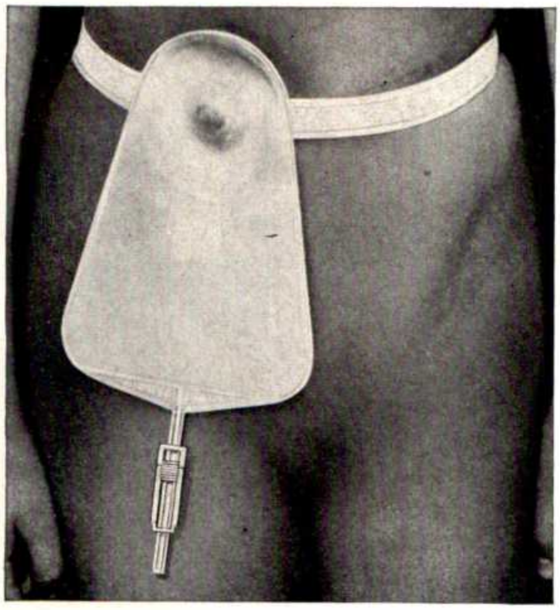

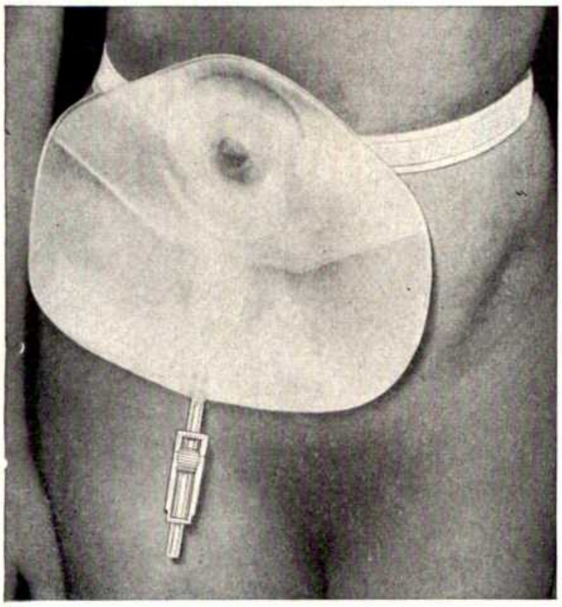

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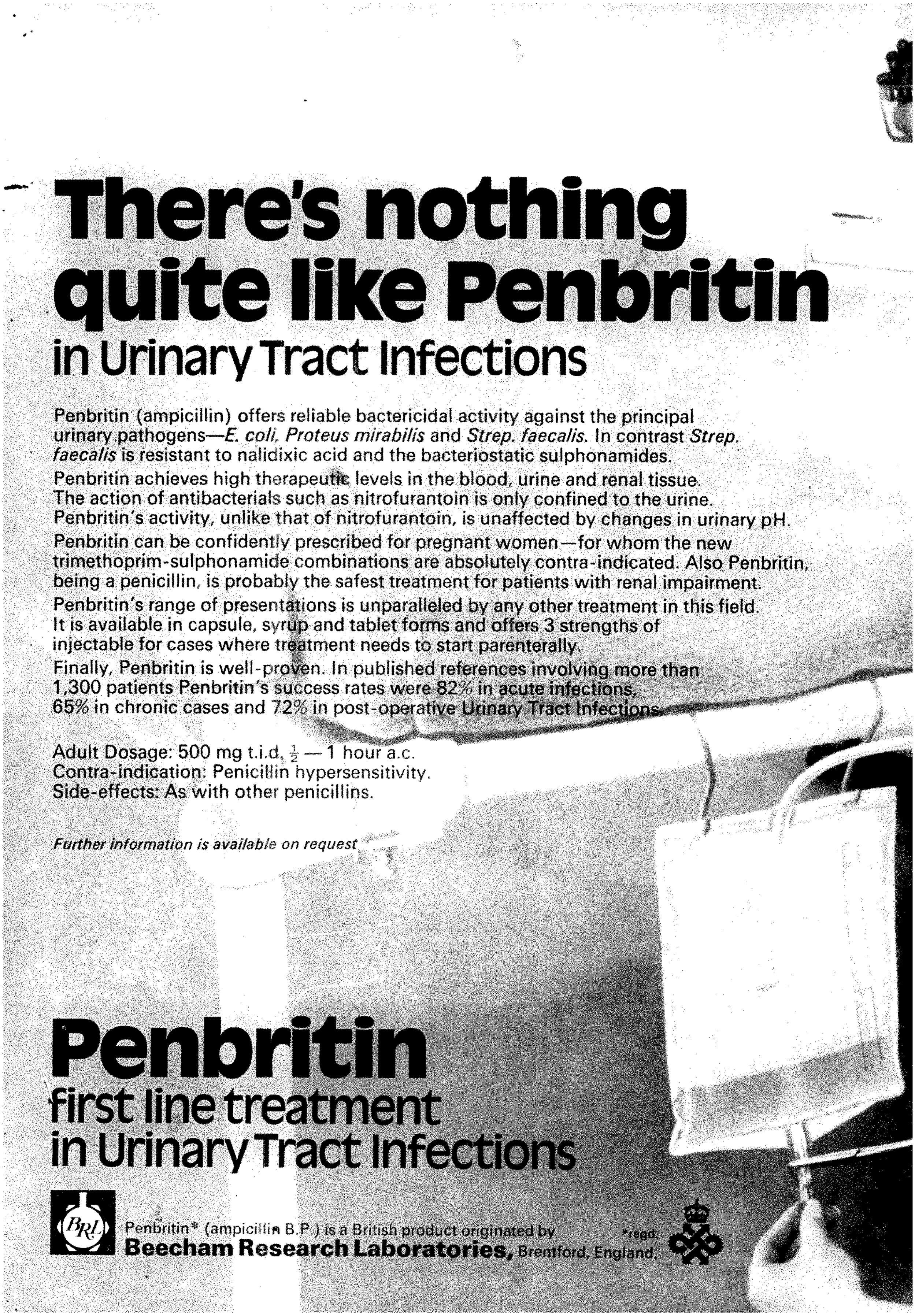

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3. *Brit med J*, (1969), **1**, 541.
4. Leading Article, *Brit med J*, (1969), **1**, 525.
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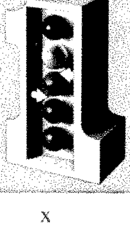

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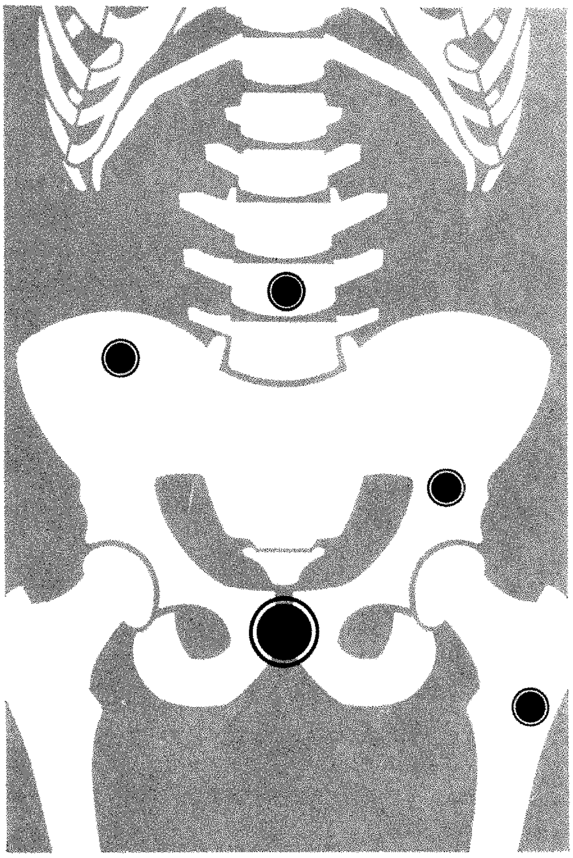

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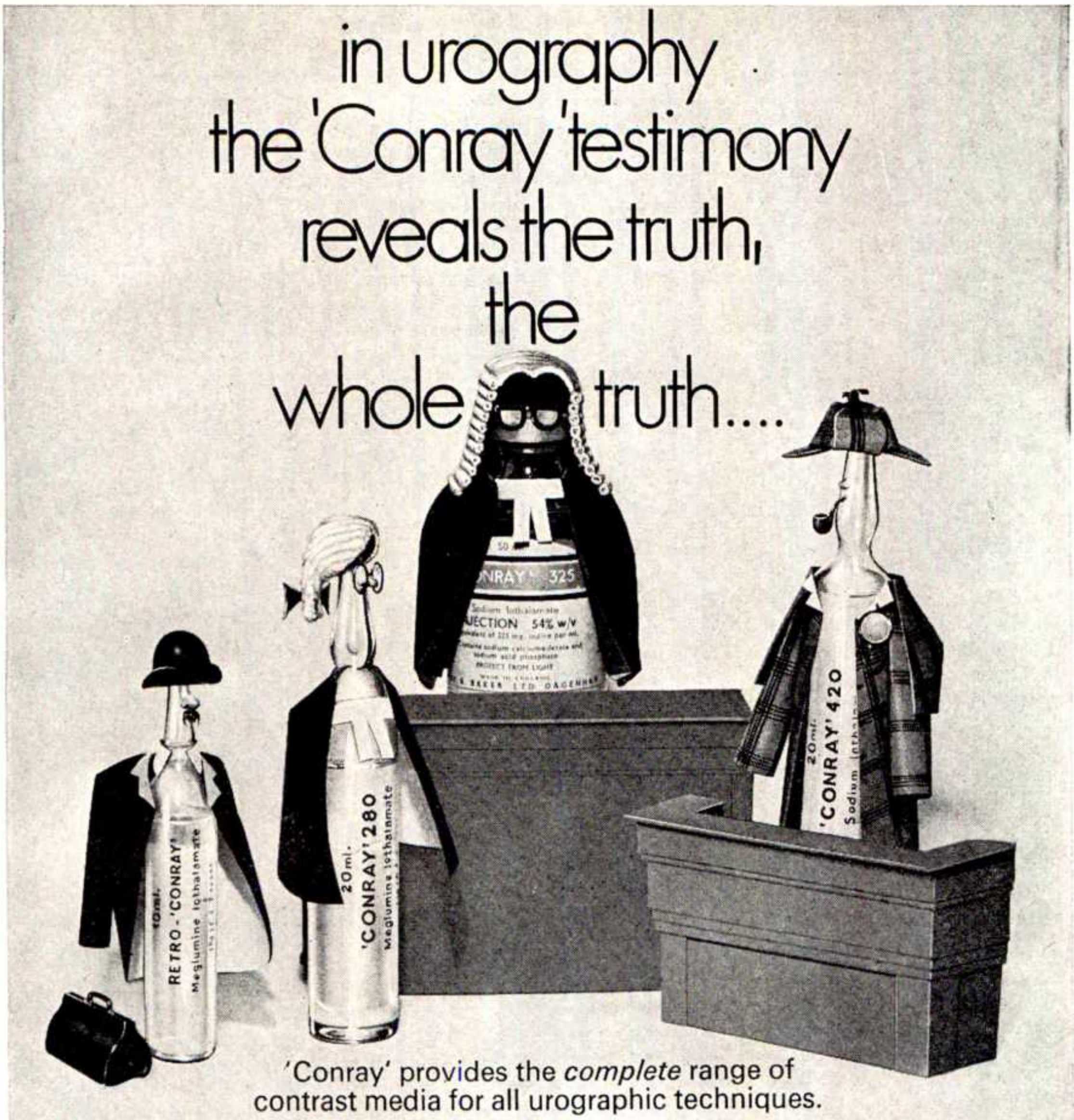

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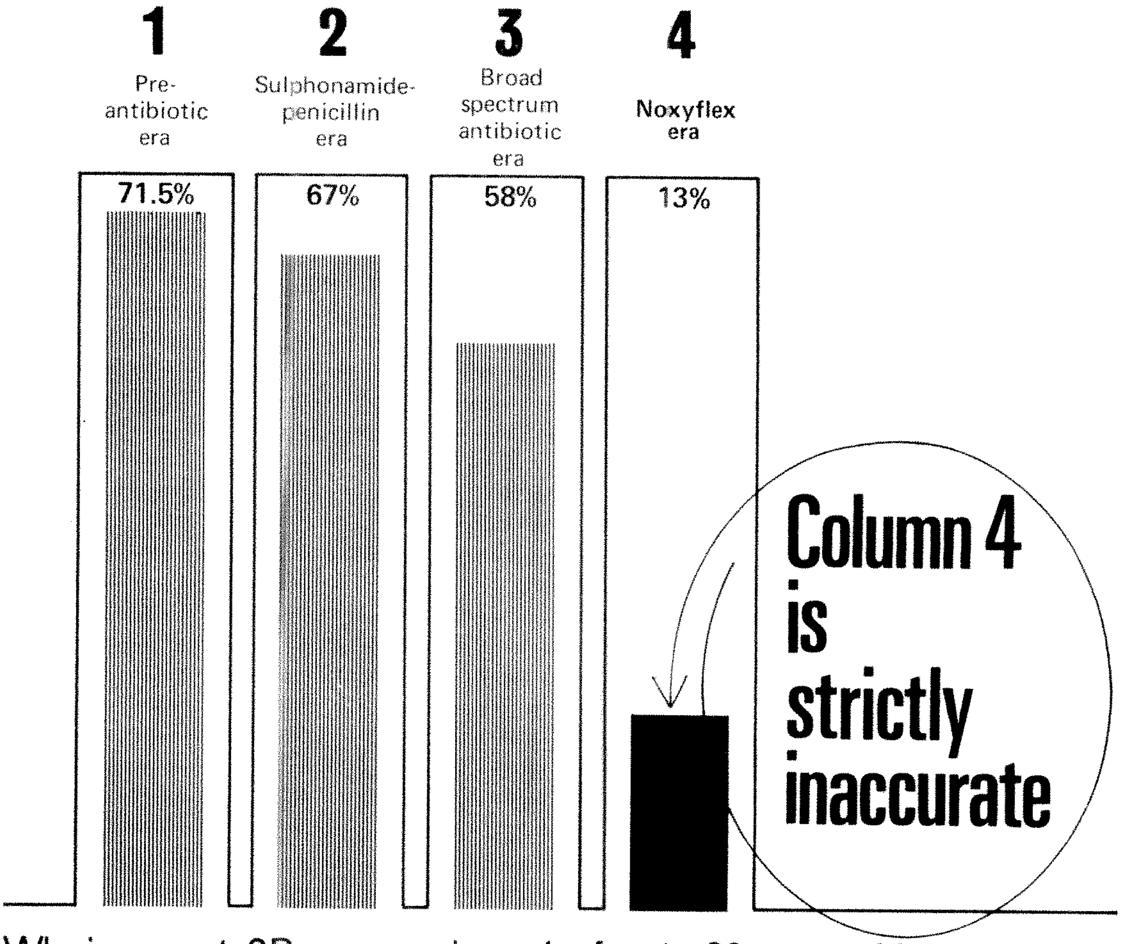

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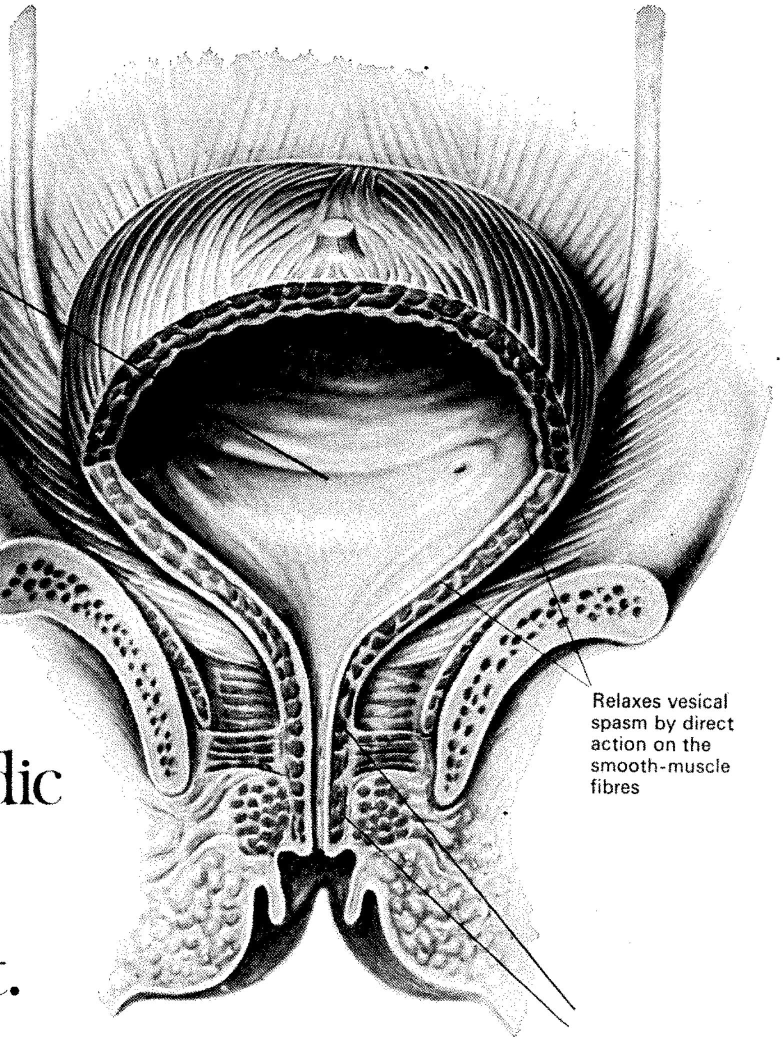
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1. *E.D.T.A. Proceedings*, VOL VI; (1969). 2. *British Journal of Urology*, (1970) **42**; 246. 3. *British Medical Journal*, (1969) **IV**; 717. 4. *British Journal of Urology*, (1970) **42**; 590. 5. *Lancet*, (1963) **ii**; 1143. 6. *J.clin.Path.*, (1964) **17**; 362. 7. Paper presented to the Dutch Ophthalmological Congress, Amsterdam, 1970. 8. *Lancet*,(1970) **ii**; 1116. 9. *J.clin.Path.*,(1964) **17**; 355. 10. *Arch.Dis.Childh.*, (1965) **40**; 235.

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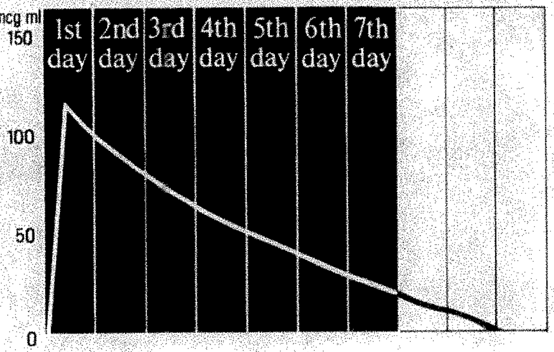

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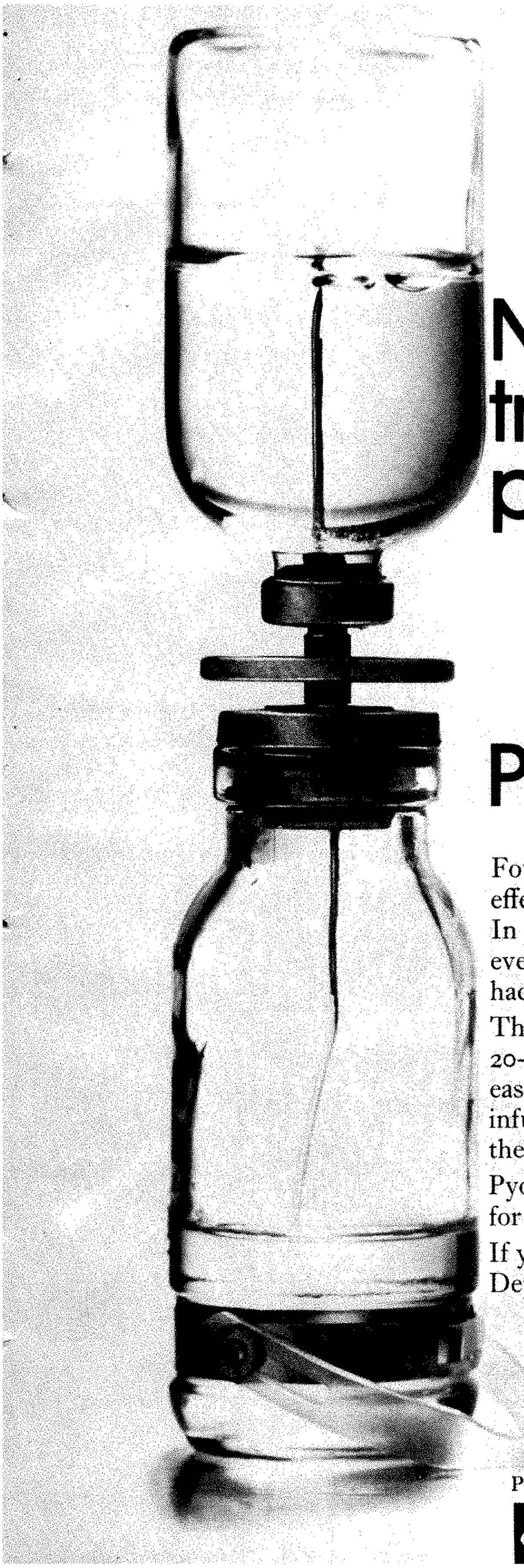

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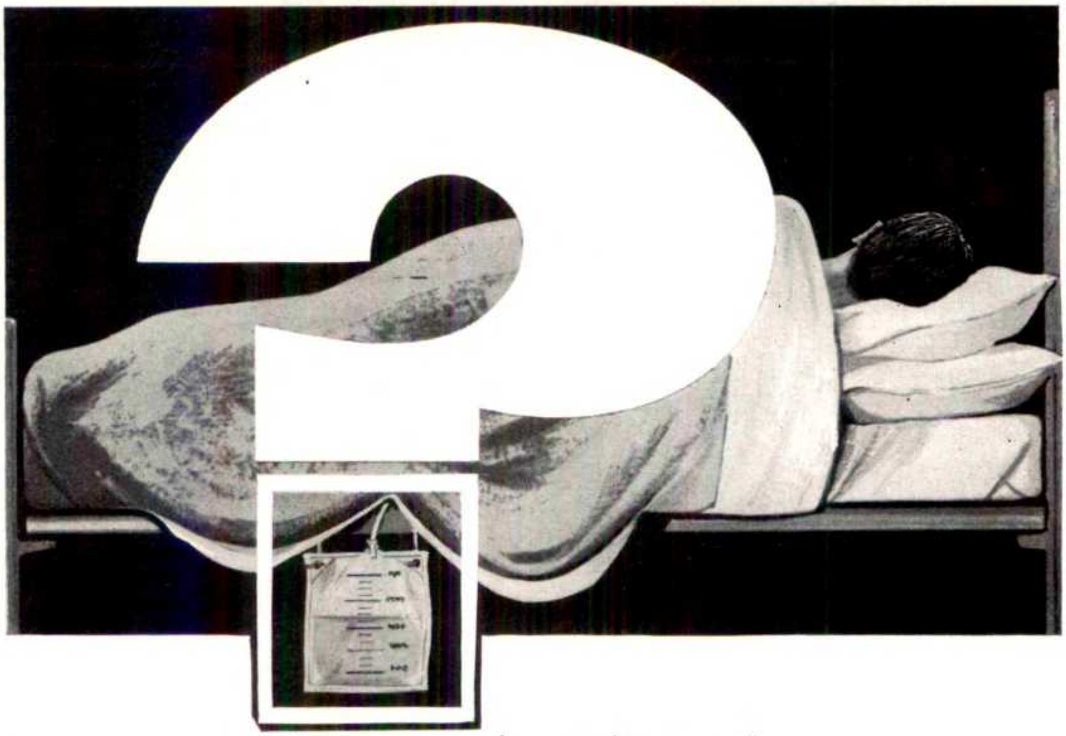

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British Journal of Urology (1972), **44**, 1-8

CONSERVATION OF THE KIDNEY IN OPERATIONS FOR TUMOURS OF THE RENAL PELVIS AND CALYCES: A REPORT OF 26 CASES[1]

By SAVA D. PETKOVIĆ

Professor of Urology, Urological Clinic, Medical Faculty, University of Belgrade, Yugoslavia

IN the last 20 years we have had the unpleasant advantage of being able to observe a large number of cases of tumours of the renal pelvis and ureter.

Table I shows the material observed in the Urological Clinic compared with tumours of the renal parenchyma.

TABLE I

Period	Kidney Parenchyma	Kidney Pelvis	Ureter
1921-1943	26	3	2
1944-1952	62	4	9
1953-1960	89	72	27
1961-1970	116	142	78
	293	221	116

The increase and frequency of the appearance of the kidney pelvis and ureteral tumours became particularly obvious about 1953. The number of cases of these tumours has increased since then and they now appear more frequently than tumours of the renal parenchyma. From personal communications (Puigvert, Barcelona; Nagel, Berlin; Alkin, Hamburg; and Bracci, Rome), it seems that kidney pelvis and ureteral tumours have been appearing in the last 2 decades more frequently all over the Continent.

TABLE II

Authors	Tumours of Kidney Pelvis	Tumours of Kidney Parenchyma	%
Albarran-Imbert (1903)	42	505	7·0
Hunt (1927)	23	318	7·0
Bell (autopsies, 1946)	7	149	4·5
Caulc (collective, 1937)	...	1,785	8·5
Riches (collective, 1951)	189	1,935	9·0
Petković (1970)	220	293	42·0

Whilst the relative incidence of kidney pelvis tumours to those of the parenchyma is generally around 8 per cent (7 per cent Albarran, 1903; 9 per cent Riches, 1951), the incidence in the Belgrade Urological Clinic is 42 per cent. From 1961 to 1970 the incidence of kidney pelvis tumours exceeded that of the renal parenchyma tumours (Table II).

From an inquiry among our colleagues in Yugoslavia we have succeeded in collecting for our statistics almost all the cases observed in the country in the last 20 years. To the end of 1970 the number of cases totalled 450 cases of renal pelvis tumours (Belgrade Urological Clinic, 220) and 257 cases of ureteral tumours (Belgrade Urological Clinic, 116). As it seemed that a particular frequency of these tumours corresponded to certain regions of Yugoslavia we plotted the geographical distribution of all the 707 cases according to the patient's usual place of residence.

---

[1] Read at the Twenty-seventh Annual Meeting of the British Association of Urological Surgeons in London, June 1971.

Some villages along particular rivers (Sava, Drina, Kolubara, Morava, Mlava) have 1 case of kidney pelvis tumour per 200 inhabitants (the village Cvetovac) or even 1 per 157 (the village Petka), while in towns only 1 case of this tumour is seen per 22,000 (Belgrade) or even 45,000 (Novi Sad) inhabitants, as Table III clearly shows.

TABLE III

	Population	Tumour Kidney Pelvis and Ureter	Incidence
Cvetovac . .	1,338	7	1/200
Petka . .	943	6	1/157
Sopići . .	1,927	9	1/222
Belgrade . .	1,000,000	46	1/22,000
Novi Sad . .	180,000	4	1/45,000
Subotica . .	80,000	2	1/40,000

In the same regions and villages we have noticed the appearance of a special chronic nephropathy called endemic nephropathy or " Balkan Nephropathy ". This nephropathy has been the subject of particular researches; we are here concerned only with its correlation with our tumour cases. A large number of our patients with tumours show symptoms of this nephropathy, by the gradual development of renal insufficiency, only mild proteinuria and a progressive and inevitable lethal course, but without hypertension.

We are now inclined to consider that this is caused by a toxic agent in the particular regions from the food or water.

TABLE IV

Tumours	Total	With Renal Insufficiency	From Endemic Nephropathy Regions	Other Regions
Kidney pelvis .	220	98 (45%)	54:98 = 54%	44:121 = 36%
Ureter . .	116	56 (48%)	27:43 = 63%	29: 73 = 40%

There is, however, an increase in the number of these tumours in other regions as well—much more than is observed with other tumours. The kidney pelvis tumours in those other regions are also accompanied by renal insufficiency, though with a lower incidence than in those cases in the regions where nephropathy is endemic.

A considerable number of our cases of renal pelvis tumours and ureteral tumours are bilateral. In our series of 336 tumours, 34 (10 per cent) were bilateral.

The first important factor making conservation of the kidney essential was the renal insufficiency in the high percentage of cases as shown in Table IV.

To our knowledge no other authors report such a high percentage of renal insufficiency in cases of these tumours; only Bloom and his collaborators (1970) reported, " Blood urea nitrogen was elevated in 42% ", which was the result of observations of 102 cases of tumours seen in 13 hospitals. This renal insufficiency necessarily modifies our indications for nephrectomy in cases of kidney pelvis and ureteral tumours.

The factors against nephrectomy are:

1. The possibility (10 per cent) of the development of a tumour on the other side.
2. Development of renal insufficiency in about 45 per cent of cases, more frequently in cases with the endemic nephropathy, less frequently in cases of tumours from other regions.
3. The large number in our series of cases of small comparatively benign tumours with a narrow pedicle, without deep infiltration.
4. It is true that conservation of the kidney carries the risk of a recurrence of the tumour at the same site or of the ureters or of the bladder. But we fear a recurrence of the tumour on the other side as much as one in the bladder if the patient's expectation of life is long.

Our indications for the conservative procedures in 26 operations were:

Absolute: Renal insufficiency (17)
Solitary kidney (5)
Bilateral tumours (7)
Relative: Small tumour with a narrow pedicle.

Ferris and Daut (1948) were the first—in 1941—to perform a renal conserving operation in a case of a renal pelvis tumour and Vest (1945) was the first to perform such an operation in a case of a ureteral tumour. In 1957 we reported conservation of the kidney in 5 cases of ureteral tumours. Küss and Quenu (1959) were decidedly against a systemic application of nephrectomy to cases of small tumours of the renal pelvis or of the ureter.

Our first conserving operation in a case of a kidney pelvis tumour was in 1962; since then we have performed similar operations in 26 cases. The results can be seen in Table V.

TABLE V

(*a*) Satisfactory results (function maintained without relapse, without uræmia)	15
(*b*) Without relapse but with uræmia	4
(*c*) Secondary nephrectomy (unsatisfactory results)	3
(*d*) Died (2 in less than a year after the operation and 2 after 2 years)	4

The length of survival after operation is shown in Table VI.

TABLE VI

(*a*) Survived over 5 years (3 with uræmia)	5
(*b*) Survived 4-5 years	3
(*c*) Survived 2-4 years	5
(*d*) Survived over 1 year	4
(*e*) Recent operation	2
(*f*) Survived with secondary nephrectomy	3
(*g*) Died	4

In the 5 cases of solitary kidneys, the other kidney had been previously removed on account of kidney pelvis or ureteral tumours. In the 17 cases with renal insufficiency before operation this was the absolute indication for the conservation. A considerable number of the tumours had no deep infiltration into the wall of the kidney pelvis and had a narrow pedicle. If the tumour covers a large part of the kidney pelvis or is infiltrating, conservation is either impossible or at least inadvisable.

The results in cases of the kidney pelvis tumours treated by nephrectomy compared with cases treated by total nephro-ureterectomy (all before 1964) are shown in Table VII.

TABLE VII

Operation	Total	Dead (after 5 years)	Alive
Nephro-ureterectomy .	47	32 (8)	15 (32%)
Nephrectomy . .	72	49 (7)	23 (32%)

If to the number of living patients we add the number of those who died more than 5 years after operation, the percentage survival over 5 years is 48 per cent.

Serious cases where conservation was essential are illustrated by the following:

Case 3.—S. E., female, age 53. Left nephrectomy in 1963 for a severe hæmorrhage (probably from tumour) in a country hospital. On 7th November 1966 a right kidney pelvis tumour and 2 small tumours of the upper part of the ureter were excised. The blood urea was normal until 1970, but now (1971) the blood urea is about 120 mg. per 100 ml. (Fig. 1).

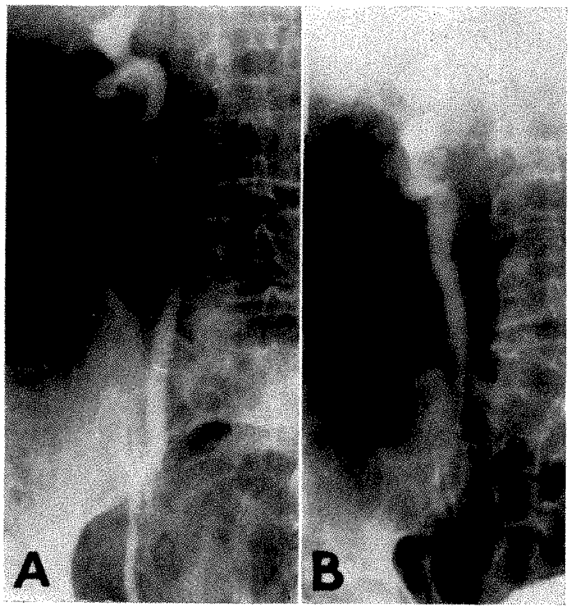

FIG. 1

Case 3. S. E. A, Pre-operative (1965): tumour in kidney pelvis and ureter of a solitary kidney. B, Post-operative follow-up April 1971: mild uraemia without recurrence of growth.

Case 4.—L. A., female, age 43. Right nephrectomy on 11th March 1964 for a carcinoma of the renal pelvis. On 8th July 1964 lower pole of the left kidney was resected for papillary carcinoma. Since 1970 the patient has been living with a blood urea of about 150 mg. per 100 ml. but in good general health.

Case 5.—K. P., female, age 49. In 1962 left nephrectomy for kidney pelvis tumour. The right superior calyx was resected on 15th May 1964 for papillary carcinoma. She was still alive in April 1971 with a blood urea of 120 mg. per 100 ml. (Fig. 2).

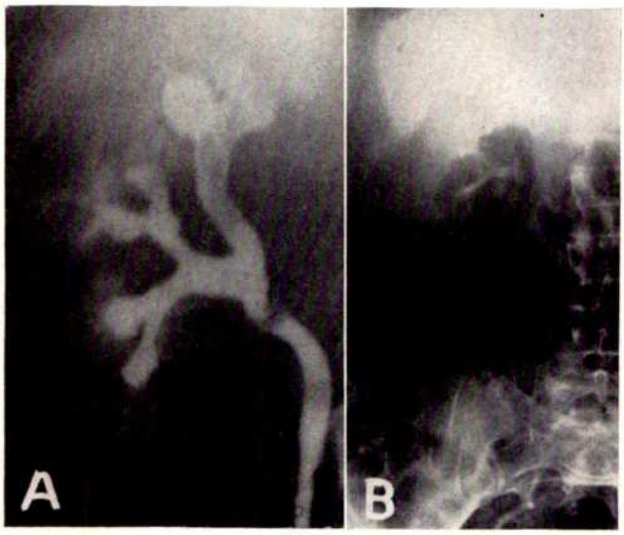

FIG. 2

Case 5. P. K. A, Pre-operative: tumour in upper calyx of right solitary kidney 1964. B, Post-operative follow-up April 1971: blood urea 62 mg. per 100 ml. No recurrence.

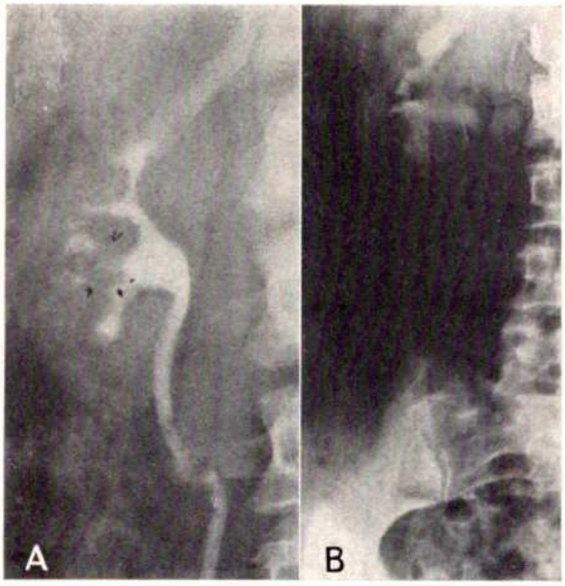

FIG. 3

Case 23. Dj. C. A, Pre-operative 1969: a small pedunculated tumour in middle calyx of right kidney. B, Post-operative follow-up in June 1971: normal blood urea. Left nephrectomy for atrophic kidney after resection of kidney pelvis for a tumour in June 1969.

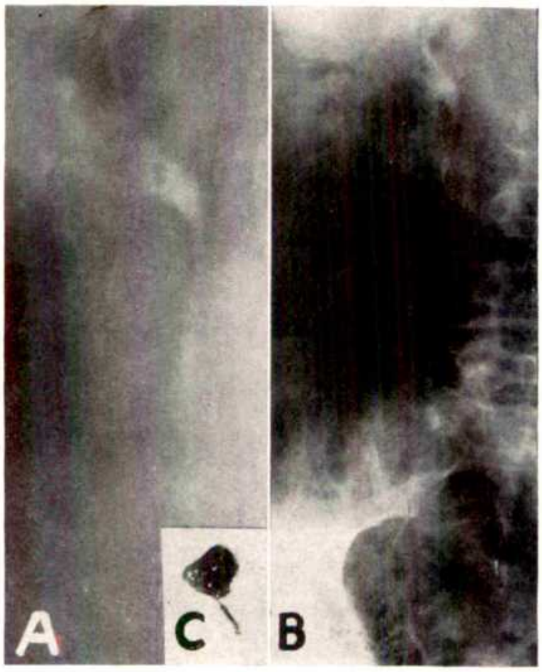

FIG. 4

Case 21. E. V. A, Pre-operative: defect in middle of kidney pelvis 1968. B, Post-operative follow-up April 1971: good kidney function. C, Extirpated tumour.

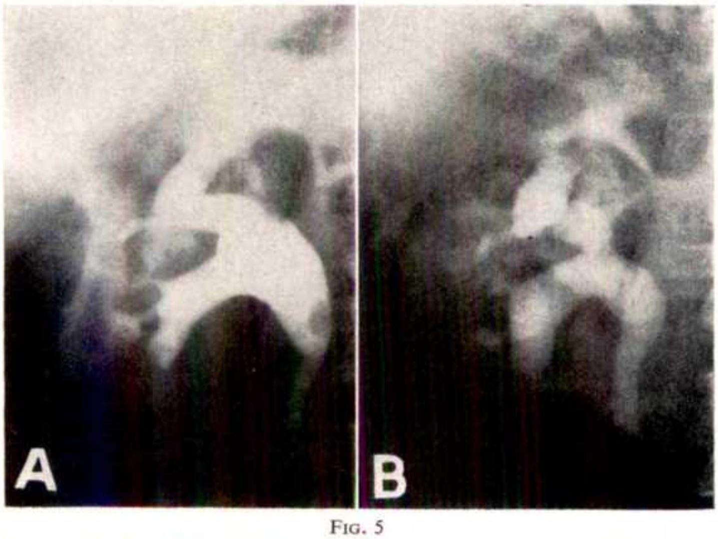

FIG. 5

Case 18. A. S. A, Pre-operative: two small tumours in the right kidney pelvis 1967 (a large tumour was present in the left kidney for which nephrectomy was performed in 1968). B, Post-operative follow-up April 1971: good kidney function.

Operative Mortality.—There has been no operative mortality in spite of 5 of the operations being on the solitary kidney.

Late Mortality.—Out of 26 patients, 4 died (2 within 1 year after operation and 2 after 2 years). The cause of death was largely renal insufficiency, but not metastases. In some cases in addition there might have been a small local recurrence.

It is noteworthy that in the series of 177 nephrectomies renal insufficiency was the cause of death as often as metastases.

Operative Technique.—This is basically quite simple but a good and wide exposure is necessary. The access to the tumour can be:

(*a*) By pyelotomy.
(*b*) By nephrotomy and wide splitting of the calyx.
(*c*) By partial nephrectomy required where the tumour involves a calyx or if early infiltration is suspected.

The exposure must provide a good view for excision of the base of the tumour. The pedicle must not be pulled off unless its base is visible; adequate access through the kidney pelvis alone is impossible if the base of the tumour lies deep in the calyx.

Throughout operation the neighbouring tissues are covered by gauze soaked in a disinfectant (Cetavlon 2 per cent solution) to protect them from implantation by tumour cells. There were no recurrences in the peri-renal tissue after these procedures.

SUMMARY

There is a vast number of kidney pelvis and ureteral tumours in Yugoslavia. They arise particularly frequently in the regions where an endemic nephropathy occurs and develop in association with this which leads to slowly progressive renal insufficiency. In about 40 per cent of the tumours in our series there is renal insufficiency. In about 10 per cent of cases the tumours are bilateral. A considerable proportion of the cases have small tumours on narrow pedicles. These were considered decisive reasons for operations conserving the kidney.

In 26 cases of tumours of the renal pelvis or of the calyx only the tumours were removed, the kidney being conserved.

The results are encouraging.

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DISCUSSION

Sir Eric Riches (London) could not recall any bilateral cases in the B.A.U.S. series of 1951. In Macalpine's series there was only one case and that was in a dye worker. In his own series of 63 cases (43 males, 20 females) there were no bilateral cases but in 15 the kidney, ureter and bladder were affected. He therefore preferred radical removal of the kidney and ureter with part of the bladder.

He thought that Dr Petković had done a valuable service in drawing attention to the endemic nephropathy of the Balkans; it appeared to be a precursor of tumours of the renal pelvis and ureter with which we were unfamiliar.

He also emphasised the need for investigation of the upper urinary tract in all cases of papillary tumour of the bladder.

British Journal of Urology (1972), **44**, 9-14

ERRORS AND PITFALLS IN THE MANAGEMENT OF ACUTE URINARY OBSTRUCTION COMPLICATED BY URÆMIA WITH SPECIAL REFERENCE TO STONE[1]

By E. PROCA

Associate Professor of Urological Surgery, Panduri Hospital, Bucharest

URÆMIC conditions are far from unusual in a urological department and often both the diagnostic and therapeutic problems they present are not easily solved.

During the last 11 years (1960-1970) we have treated 1,155 cases with renal failure from a total number of 31,671 patients admitted to our hospital (Fig. 1).

In nearly half of these patients (461 cases) the uræmia was related to acute tubular necrosis and will not be analysed in this paper.

In the other 654 patients (who had blood urea levels greater than 70 mg. per 100 ml. when admitted) the uræmia was related to mechanical obstruction of the urinary passages (Fig. 2).

Compared with the reversible renal failure accompanying acute tubular necrosis or the relentlessly progressive course of nephrosclerosis, obstructive uræmia has some definite features:

1. It occurs late in the evolution of urinary disease.
2. Its development is characterised by fluctuations associated with either acute temporary obstruction or exacerbations of pyelonephritis.
3. The urinary output is usually preserved.
4. Surgery plays a definite part in the management.
5. Sudden anuria may be the first clinical symptom of a long, silent history of urinary tract obstruction.

In this paper the discussion will be restricted to the errors and pitfalls we have encountered in the management of calculous anuria and bilateral obstructive nephrolithiasis.

Calculous Anuria.—In this group there were 80 patients. All of them were admitted with complete anuria and various degrees of uræmia: 51 (63 per cent) patients had blood urea levels less than 200 mg. per 100 ml. and were considered to be in the so-called clinical " tolerance " phase of uræmia, while 29 patients (37 per cent) had blood urea levels within the range of 200-680 mg. per 100 ml.—with a mean value of 348 mg. per 100 ml.—and presented severe symptoms of uræmic intoxication.

In all our cases the anuria was exclusively due to mechanical obstruction of the urinary tract: 20 patients had bilateral stones either in the renal pelvis (15 cases) or in the ureters (5 cases) while 60 patients had a single functioning kidney with calculous obstruction: in 22 patients the contralateral kidney had been previously removed (in 19 for stones, in 3 for tuberculosis) and in the other 38 patients the other kidney was functionless.

Only 11 of these 38 patients were aware that they had a non-functioning kidney. In the other 27 patients, it was anuria that revealed for the first time the existence of a silently destroyed contralateral kidney (25 cases) or its congenital absence (2 cases) (Fig. 3).

We have never encountered the so-called calculous reflex anuria and consequently very much doubt its existence.

Emergency relief of the obstruction either surgically or by means of an indwelling ureteral catheter is obviously required.

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[1] Read at the Twenty-seventh Annual Meeting of the British Association of Urological Surgeons in London, June 1971.

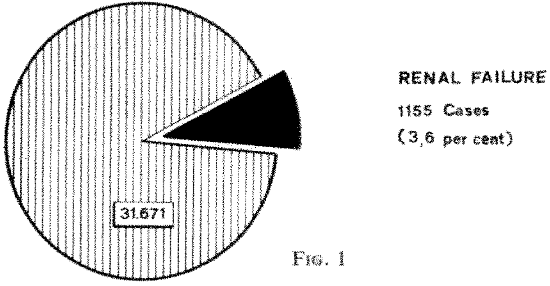

FIG. 1

Fig. 1.—Total number of patients admitted during the last 11 years (1960-1970) compared with the number of renal failure cases.

Fig. 2.—Number of patients with obstructive uræmia.

Fig. 3.—Calculous anuria: 80 cases.

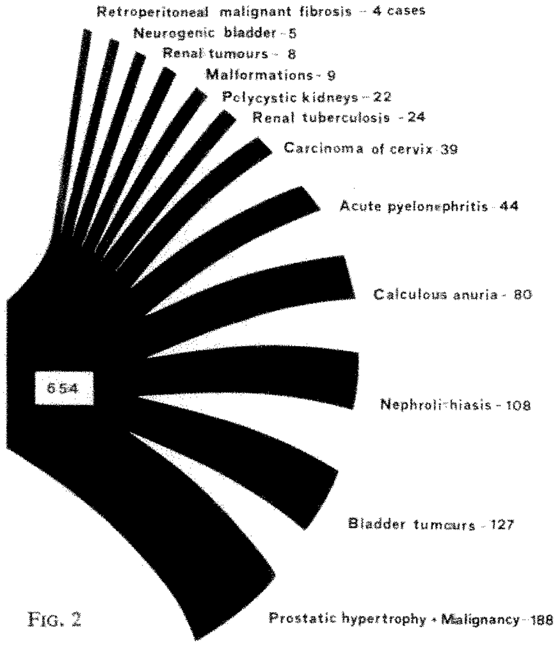

FIG. 2

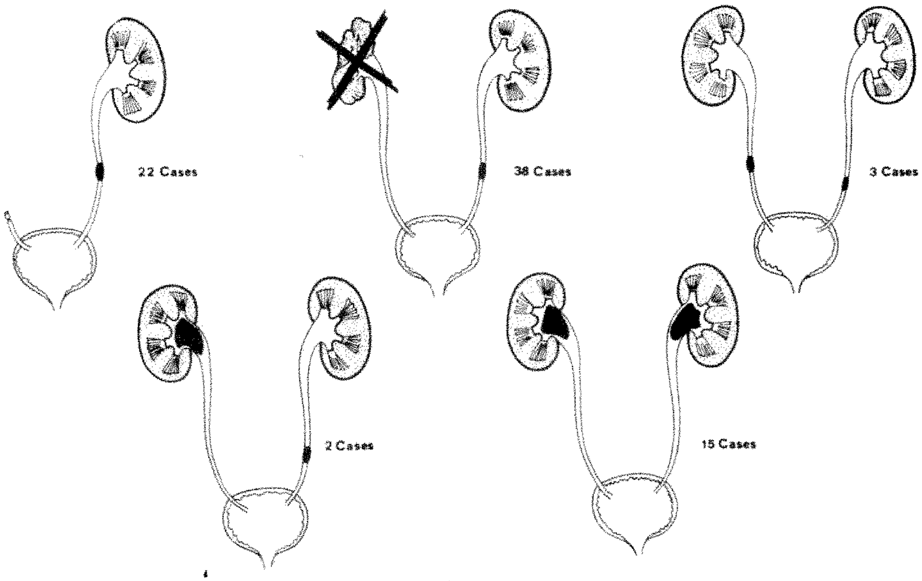

FIG. 3

Our policy in these cases consisted of:

1. If the patient was admitted in good condition with mild uræmia and was a good operative risk, the urinary obstruction was relieved forthwith by surgical removal of the calculus provided the site of obstruction was known beforehand, *e.g.* by the stone being radio-opaque.

Whenever the renal calyces were grossly dilated and/or the urine was infected, the surgical procedure concluded with a temporary drainage procedure—nephrostomy when the kidney was in the operative field, or ureterostomy *in situ*. When the stone was radiolucent and/or could not be located on the plain film, the site of obstruction was determined by ureteric catheterisation and the surgical approach selected accordingly.

2. If the patient was admitted with severe uræmic intoxication, we usually tried to restore the urinary flow by means of ureteric catheterisation. If this attempt failed, a temporary drainage procedure, usually nephrostomy—under local anæsthesia if necessary—was performed.

A number of patients were operated on after initial hæmodialysis. Our results are presented in Table I.

TABLE I

Calculous Anuria: Results in 80 Patients

PROCEDURE	NUMBER OF CASES				
	Single Functioning Kidney	Single Surgical Kidney	Bilateral Kidney Stones	Bilateral Ureteric Stones	Combined Kidney + Ureteric Stones
Ureteral Catheterisation	11 < 1d / 10c	3 < c	5 < 1d / 4c		
Ureteral Catheterisation + Haemodialysis	1 < 1c	1 < 1c			
Ureteral Catheterisation + Surgery	7 < 2d / 5c	9 < 2d / 7c			
Haemodialysis		1 < 1d	1 < 1d		
Haemodialysis + Surgery	4 < 1d / 3c		5 < 3d / 2c	1 < 1d	
Surgery	11 < 3d / 8c	7 < 1d / 6c	4 < 1d / 3c	2 < 2c	2 < 2c
Spontaneous Elimination	4 < 4c	1 < 1c			
	38 < 7d / 31c	22 < 4d / 18c	15 < 6d / 9c	3 < 1d / 2c	2 < 2c

18 died [23 per cent]
TOTAL NUMBER — 80 CASES :
d = died
62 cured [77 per cent]
c = cured

Except for some indisputable successes, this policy was subject to pitfalls and errors which will be analysed later.

Ureteric Catheterisation.—This was used in 37 patients either alone (19 cases—17 relieved, 2 died), or in combination with hæmodialysis (2 cases—both relieved) or with surgery (16 cases—12 relieved, 4 died).

Undoubtedly for a quick and easy relief of urinary obstruction this procedure may be of great value. However, the following unsatisfactory situations may arise:

(*a*) The ureteric catheter may fail to pass beyond the site of obstruction, yet surgical relief is illogically postponed and on the days following other attempts at ureteric catheterisation are made which may favour ascending infection and renal deterioration.

(*b*) The ureteric catheter does succeed in relieving the obstruction but is maintained indwelling for too long. Urinary infection is consequently almost unavoidable, sometimes taking the form of acute pyelonephritis, with recurrence of the uræmia.

In our series 8 patients had long-lasting pyelonephritis after ureteric catheterisation, despite the fact that they subsequently eliminated the calculus.

(*c*) The ureteric catheter may give false information concerning the site of obstruction in the case of a non-opaque stone. For example, it may be arrested in the lower segment of the ureter, when the stone is actually impacted in the uretero-pelvic junction thus leading to an unsuitable approach.

In 3 of our cases we erroneously opened the abdominal wall through Key's subumbilical midline incision when the stones were located in the upper ureter.

(*d*) The improvement brought about by ureteric catheterisation is easily reversed; the catheter may become obstructed and the anuria recur when the catheter is removed.

In 16 of our cases we were forced to remove a blocked catheter and to resort to surgery.

Surgery.—Fifty-two patients underwent open surgical procedures. In 26 cases the surgical procedure was performed as an emergency (5 died), in 10 cases surgery was associated with hæmodialysis (5 died), and 16 patients had an indwelling ureteric catheter before surgery (4 died).

The mortality rate in this group was 25 per cent (13 patients).

TABLE II

Calculous Anuria—Surgical Treatment and Results in 52 Patients

Technical Procedure	Number of Cases	Number of Cases: Surgery+Dialysis	Number of Deceased Cases
Ureterolithotomy	25	1	4
In situ ureterostomy	2	1	...
Pyelolithotomy	8	...	2
Pyelolithotomy+Pyelostomy . . .	3	2	...
Nephrostomy	10	2	6
Nephrolithotomy+Nephrostomy . . .	3	1	...
Pyeloplasty	1	1	1
	52	8	13 (25%)

In Table II the procedures and results are shown.

Undoubtedly surgery has a higher risk when performed on a uræmic patient, but it may be life-saving when properly indicated and executed.

The greatest error one can make in this respect is not to operate on a patient in a well-tolerated clinical phase of uræmia and either to waste time waiting for spontaneous elimination of a ureteric calculus or to rely too much on the ureteric catheter. The consequences of postponing surgery may be having to undertake a more hazardous procedure on a patient in a much poorer condition. Of the 18 patients who died, 16 were in the group with severe uræmia.

Another surgical error consists of performing surgery in good time, but ending the operation without providing proper relief of urinary obstruction.

Three patients were referred for hæmodialysis with grossly distended kidneys and acute pyelonephritis because at a previous operation neither had the obstructive calculus been removed nor had tube drainage been instituted. Nephrostomy and dialysis were carried out but all died in bacteræmic shock.

A difficult problem is presented by those uræmic patients whose calculi on radiography do not seem to be definitely obstructing the urinary tract. Our impression is that operative procedures are rarely indicated in such cases which belong rather to the province of the nephrologist. The ureteric catheter may be most valuable in identifying these cases; if ureteric catheter drainage does not improve the urinary drainage, surgery will be of no avail.

The unwary surgeon may, however, be tempted to do a radical but time-consuming and dangerous operation instead of performing a quick and less aggressive one. We regret performing a pyeloplasty instead of a life-saving nephrostomy in a patient with acute pelvi-ureteric obstruction in a solitary kidney with uræmia which had been temporarily controlled by hæmodialysis.

Bilateral Obstructive Nephrolithiasis and Advanced Uræmia.— Out of a total of 304 patients with bilateral nephrolithiasis, 196 had a normal blood urea; in 85 cases it was higher than 70 mg per 100 ml. and 23 patients were admitted with advanced uræmia with the blood urea higher than 100 mg. per 100 ml. and with the creatinine clearance below 40 ml. per minute (Table III).

TABLE III

Bilateral Obstructive Nephrolithiasis and Uræmia

Normal blood urea	196 cases	
Blood urea 70 mg. per 100 ml.	85 cases	108
Blood urea 100 mg. per 100 ml.	23 cases	
	304 cases	

Only the 23 severely uræmic patients will be analysed here.

All of them had bilateral multiple kidney stones and a clinical course extending over many years. As long as their kidney function tests remained normal surgery had been deemed unnecessary and as soon as they became uræmic surgery had been considered both useless and risky.

For many years such patients had been abandoned to an apparently unavoidable death. However, the advent of hæmodialysis has given rise to new hope and has obliged us to change our attitude.

In the group of 23, 8 patients were treated conservatively; 7 died and only 1 was improved by hæmodialysis alone.

The other 15 patients were operated upon under the protection of hæmodialysis. This resulted in surprisingly good and lasting benefit in 7, but the remaining 8 died.

Nevertheless, these results may be considered as a convincing plea for a more active surgical approach in bilateral renal lithiasis complicated by uræmia.

Since hæmodialysis can turn a very poor risk patient into an acceptable one and lower the post-operative mortality, renal insufficiency can no longer be considered as a contra-indication to operation for bilateral renal lithiasis. In fact, surgery performed with certain precautions and under the protection of dialysis is the essential factor in the recovery of renal function. One should not forget that in such cases potentially reversible renal lesions almost always exist and the renal parenchyma has surprising resources of recovery, provided that the obstruction is relieved and the infection is controlled.

SUMMARY

Six hundred and fifty-four patients with obstructive uræmia are reviewed, with special emphasis on calculous anuria and bilateral nephrolithiasis complicated by blood nitrogen retention.

Some errors and pitfalls in the management of acute obstructive uræmia are discussed, followed by a brief analysis of the results obtained in the treatment of bilateral kidney stones and renal failure.

Such cases should no longer be abandoned, because surgery performed under protection of hæmodialysis can often provide unexpectedly good results.

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DISCUSSION

Sir Eric Riches (London) favoured nephrostomy as a preliminary to surgical correction and referred to a patient aged 26 in Pakistan treated in 1957 when no dialysis was available. He had anuria with a blood urea of 220 mg. per cent from gross bilateral hydronephrosis. Right nephrostomy had enabled him to come to England where bilateral plastic operations were done. The kidneys remained enlarged and infected but he was working and leading a normal life 14 years later; the blood urea in 1971 was 40 mg. per cent.

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LATE RESULTS IN THE MANAGEMENT OF PRIMARY PELVIC HYDRONEPHROSIS[1]

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THE first decision which faces the surgeon treating a patient with pelvic hydronephrosis is whether surgical intervention is justifiable. Surgery may be indicated if the symptoms demand it or, alternatively, if there is evidence of progressive disease or significant complication of the primary lesion. We have previously reported our views on the natural history of this condition (Roberts and Slade, 1964) and have concluded that surgery is, in many cases, justified. Our conclusion was based on the evidence of assessment of 2 groups of patients.

The first group consisted of patients who had either a symptomless hydronephrosis discovered during the investigation of other symptoms or one of modest dimensions but producing symptoms, usually of loin pain. Twenty-six such patients were followed up in the out-patient clinic with serial bacteriological and radiological studies for periods of 1 to 20 years. Only 6 patients in this group showed no evidence of deterioration in the state of the affected kidney and of these 2 insisted upon surgical intervention because of the amount of pain they suffered. In the remaining 4 patients the follow-up was for less than 3 years. This provided strong support for surgical intervention in such patients, or at least demonstrated the absolute necessity for long-term follow-up if surgery is not contemplated. The patient in whom conservative management may, perhaps, be most considered is the one with a large extra-renal pelvis. Extra-renal dilatation often appears to spare the renal parenchyma the effects of back pressure.

The second group investigated consisted of 30 patients who had died from a variety of causes and had been found at autopsy to have a pelvic hydronephrosis in one or both kidneys. This condition had been unsuspected during life. If it had been found that the majority of involved kidneys showed only minimal changes of the effects of obstruction and infection, argument for conservative management would thereby have been strengthened. However, 14 of the 30 kidneys at risk showed extensive damage whilst in a further 13 there was considerable dilatation of the pelvi-calyceal system although the renal parenchyma was still tolerably well preserved. Stone formation had taken place in 4 patients, tumour formation in 1 and hydronephrosis had been the cause of death in a further 3. Such evidence further convinced us of the wisdom of surgical intervention in the majority of patients with primary pelvic hydronephrosis.

Having then made the major decision to operate, especially if the condition is complicated by stone or infection and absolutely if complicated by tumour formation, it was felt necessary to see if the results of surgical management in the Bristol centre were any better than the absence of treatment could produce.

Having opted for surgery the next major decision to be made is whether to remove the involved kidney or to attempt to conserve it by one of the many described procedures. We were largely influenced in this decision by the high incidence of bilateral disease varying in reported series from 15 to 50 per cent (Anderson, 1953). Though obvious radiological hydronephrosis was seen bilaterally in approximately 15 per cent of our series, if one is to believe the results of renography the true incidence of bilateral change is probably nearer to 50 per cent. Furthermore, experience with 5 patients who had presented to the Department with anuria due to acute retention of a solitary hydronephrotic kidney, having had the original kidney removed for the same pathology, made it difficult not to have one's opinions coloured by these therapeutic crises. We have, therefore, agreed with other workers in this field that attempts should be made to conserve a hydronephrotic kidney even when the opposite one appears to be normal. This decision has been further strengthened by the knowledge of the significant incidence of other associated congenital anomalies elsewhere within the urinary tract (Table).

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[1] Read at the Twenty-seventh Annual Meeting of the British Association of Urological Surgeons in London, June 1971.

TABLE

Pelvic Hydronephrosis (200 Cases)

Associated Congenital Urinary Anomalies in 16 Cases

Horseshoe kidney		4
Double kidney	Ipsilateral	3
	Contralateral	3
Ureterocoele		2
Contralateral agenesis		3
Stricture lower end contralateral ureter		1

Finally, whilst still lacking absolute proof of the hypothesis, it is suspected that as the obstructed and damaged kidney loses its concentrating power so it comes to deal with more than half of the excreted urinary output, albeit in a dilute form. Nephrectomy may then more than double the urinary output in the remaining pelvi-calyceal system which may in turn break down and become hydronephrotic under conditions of such a substantial fluid load. This phenomenon is well recognised since the use of pyelography under conditions of diuresis. Nephrectomy may thus increase the risk of hydronephrosis in the contralateral kidney to a degree which would not occur if a conservative procedure had been carried out.

These arguments of necessity assume that operations aimed at preservation of the kidney and relief of the obstruction are sufficiently successful to merit their continued use. In order to assess the truth of this statement we have, therefore, surveyed a group of patients treated by such operations (most commonly the Anderson-Hynes type of procedure, but also increasingly over recent years Culp-type operations and occasionally Davies intubation procedures). All these patients have been observed for at least 3 years post-operatively and some of them for 10 or 15 years. The operations were performed by several surgeons so the details of the techniques have varied: thus, for example, intubation of the anastomosis was a common but not invariable procedure. The follow-up has regrettably been by no means complete and approximately one-third of the patients submitted to pyeloplasty have not been traced for re-assessment.

The assessment was not easy as the obvious factor to investigate initially is the effect of any operative procedure on renal function. Most surgeons, however, are well aware of the problems of accurate assessment of renal function in the presence of a normal contralateral kidney. Differential renal function tests have in our hands been sufficiently disappointing not to merit the stress imposed upon both patients and staff, and were not undertaken. Operations on a solitary kidney, at times in an anuric patient, have demonstrated that substantial improvement is possible as evidenced by falling blood urea and increasing creatinine clearance, but we do not know if this is equally true in the presence of a second and normal kidney. The factors most easily assessed were the relief of symptoms caused by the hydronephrosis, the change in the size of the dilated calyces and the improvement in the drainage from the pelvis to the ureter. Considering even these criteria, there was still no absolute answer produced by this survey. The results are presented for 75 operations adequately followed for a minimum of at least 3 years.

Relief of pain, if present, is obviously of importance and is happily almost invariably obtained even though the other aspects of the repair may be less successful. It seems possible that the dissection of the renal pelvis produces an efficient renal denervation which accounts for the loss of pain, though this may return later if secondary stone formation occurs. Only 3 of the 75 patients complained of post-operative loin pain.

Radiologically significant improvement of the calyceal size (Fig. 1) was disappointingly uncommon and was seen after only 15 of the 75 operations. The chances of such improvement occurring was better in younger patients and when the urinary tract remained sterile. Furthermore the changes were often slow to develop and on one occasion were apparent at a 10-year follow-up when 5 years previously the radiological result had appeared to be disappointing.

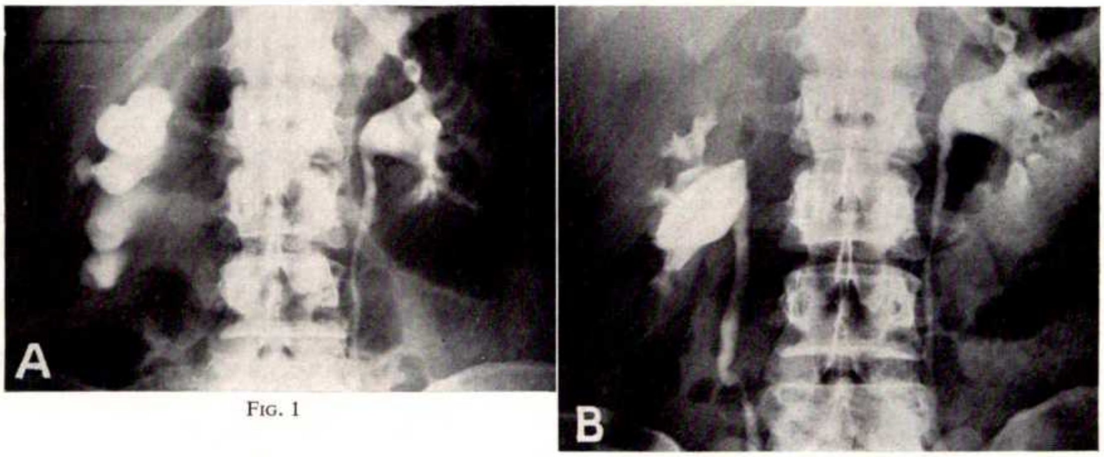

FIG. 1

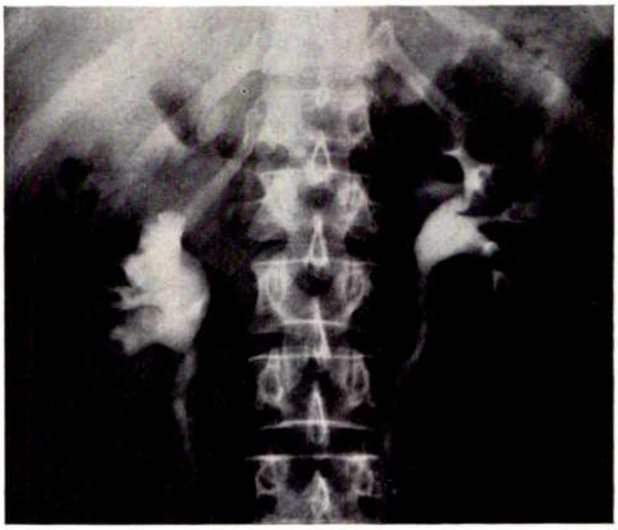

FIG. 2

Fig. 1.—A, Pre-operative urogram. B, Post-operative urogram. Demonstrating an uncommon degree of improvement in calyceal cupping as well as good ureteric filling.

Fig. 2. — Post-pyeloplasty appearances in right kidney showing good ureteric filling but calyces still dilated when compared with the opposite side.

Improvement in drainage can be assessed either by the filling of the ureter and emptying of the pelvis at excretion urography or by renography. As is becoming increasingly apparent these two investigations produce very dissimilar results and must be assumed to assess different aspects of the urinary conducting system. Good ureteric filling (Fig. 2) was found in 65 of the 75 operations and several of the failures came to re-operation as will be mentioned later.

Isotope renography has been performed only relatively recently and generally there is surprisingly little evidence of change in the post-operative phase. Occasional cases are now appearing some 3 years after surgery when a return towards normal pattern is seen, but there is as yet insufficient evidence to comment significantly on this aspect of the follow-up—nor are we yet sure what parameter or parameters we are actually assessing in renography.

Infection was relatively uncommon in the hydronephrotic kidneys, being seen in only 45 of the 200 cases in the original 1964 series, and if there was no initially gross pyonephrosis necessitating nephrectomy, the conservative procedures were very successful in eradicating such infection as was present. It is of interest to note that in our experience pelvic hydronephrosis with proteus infection was synonymous with stone formation (Slade and Roberts, 1967).

Secondary surgery was necessary in 12 patients, 5 nephrectomies being performed for infection in 3 cases and for stone in 2. The pyeloplasty was repeated twice, once for a ring of calculi with scarring following the use of monofilament nylon suture for anastomosis and once for scarring of the pelvi-ureteric junction. Stones formed in a further 7 patients; in 4 of these the stones were deposited upon monofilament nylon used in the anastomosis and obviously unabsorbable suture should not be used for this procedure.

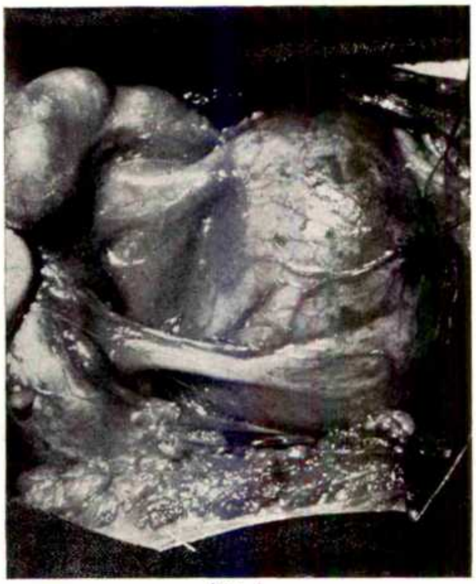

FIG. 3
Pelvic hydronephrosis with extra-renal major calyces and pelvis.

One condition which is probably not a true primary pelvic hydronephrosis, namely *the kidney with totally extra-renal pelvis and major calyces* (Fig. 3) is uncommon and such kidneys have seemed minimally affected by pyeloplasty in our experience. These may well require intervention at calyceal level as well as at the pelvi-ureteric junction.

CONCLUSIONS

In summary, our experience suggests that surgery is very commonly indicated in patients with primary pelvic hydronephrosis because of the tendency of the condition to progress to damage from back pressure, and because of the high incidence of bilateral disease. Such surgery should aim at conservation of the kidney wherever possible. This nearly always cures the patient's symptoms and infection, but may be disappointing in the radiological and renographic results especially in the short term. Long-term follow-up is recommended if surgery is undertaken, be it nephrectomy or a conservative procedure, and is even more essential if surgery is withheld.

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ACUTE TRANSURETHRAL INVERSION OF THE BLADDER ASSOCIATED WITH PROCIDENTIA

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Rectal prolapse is not uncommon but prolapse or inversion of the bladder has only lately been reported in adults. The bladder is normally retained *in situ* by its strong basal attachments and the urachal attachments to the umbilicus. In those cases in which inversion has been reported, there has always been some predisposing lesion such as vesico-vaginal fistula or ligamentous laxity in pregnancy. The patient reported here had never had a full-term pregnancy, but she had probably had local tissue damage caused by previous lymphogranuloma venereum infection, and she also had marked utero-genital prolapse.

Case Report.—The patient was a 50-year-old Muganda lady, who had reached the menopause 5 years previously. She was admitted to Mulago Hospital, Kampala, on 18th March 1970 complaining of a lump at the vulva. She gave a 1 week history of general fatigue, pain in the lower abdomen and vagina, severe diarrhœa and difficulty in micturition, being able to void only a few drops at a time.

On the day prior to admission, a mass suddenly appeared at the vulva and from that time there was complete inability to pass urine. There was no history of trauma.

In her past history there were only 2 possibly relevant points. She had been pregnant only once, 30 years previously, and this had ended in a first trimester abortion, and 10 years previously she had suffered from painful sores around the vulva and anus. These were treated with local applications for 2 weeks and she had had no trouble since.

General examination revealed no abnormality. On perineal examination there was a complete procidentia and anterior to this a large congested œdematous, pyriform mass. This was thought to be a grossly hypertrophied anterior vaginal wall, although a diagnosis of complete inversion of the bladder was entertained. There was also a " button hole " anal tag and a tight rectal stricture suggestive of previous lymphogranuloma venereum infection. Rectal examination showed the rectum to be full of fæces.

Under anæsthesia an attempt to reduce the masses was unsuccessful. An orifice on the posterior aspect of the upper mass and slightly to the right of the midline was thought to be the urethra. A Foley catheter was inserted and left *in situ*. The patient was then treated conservatively with continuous urine drainage, ice-packs to the swellings and antibiotic therapy. The hæmoglobin was 12·4 g. per cent, blood urea 83 mg. per cent and white cell count 12,600 per c.mm. After 1 week of conservative treatment the swellings were only minimally reduced. The catheter was removed and on attempting to replace it a second orifice to the left of the midline was seen to be spurting urine (Fig. 1). At this stage the diagnosis of transurethral inversion of the bladder became obvious.

As the masses could not be reduced from below, a laparotomy was performed through a Pfannenstiel incision. The fundus of the uterus was identified and pulled up into the pelvis. The inversion of the bladder was now clearly seen and appeared to have originated from the posterior wall of the urethra. The urethra, which would already admit 3 fingers from above, was nevertheless acting as a constriction ring to the grossly œdematous bladder.

Pressure bandages were applied to the inverted bladder in an effort to reduce its size. It was, however, necessary to incise the anterior urethra in order to release the constriction before the inversion could be reduced. A hysterosacral suspension was then performed to prevent the uterus from prolapsing again and a suprapubic catheter inserted into the bladder. The dome of the bladder was then fixed to the anterior abdominal wall, and the abdomen was closed in layers.

After reduction of the prolapse the underlying pathology was clear (Fig. 2). The urethra was not only dilated but had been partly destroyed by some previous disease. The lower 3 cm. was missing and from the urethral orifice, now lying well inside the vagina, 2 œdematous but epithelialised tags 2 cm. long protruded posteriorly. The constriction ring lay at the bladder neck but was not gangrenous, and the residual urethra was estimated to be about 1·5 cm. long.

The cervix was about 8 cm. long and even when the procidentia was fully reduced almost emerged at the introitus. Its epithelium was thickened but not ulcerated. The posterior vaginal wall and perineal body showed considerable scarring and now a large rectocele prolapsed through the scarred lower vagina.

It was decided to leave reconstruction of the urethra and repair of the rectocele for a later date, when the œdema and infection had subsided, and the functional state of the urethral sphincter could be properly assessed.

In spite of antibiotics the patient developed a right-sided pyelonephritis 3 weeks after operation. Pseudomonas and Klebsiella were isolated and the infection responded rapidly to Trimethoprim

The suprapubic catheter was replaced by a Foley catheter on the 12th post-operative day; the latter was discontinued on the 25th day. It was noticed at this stage that the patient was occasionally incontinent of urine in bed and there was some stress incontinence on standing. Blood urea estimation was normal and an intravenous pyelogram carried out at this stage showed a normal upper urinary tract. Frei test for lymphogranuloma venereum was negative.

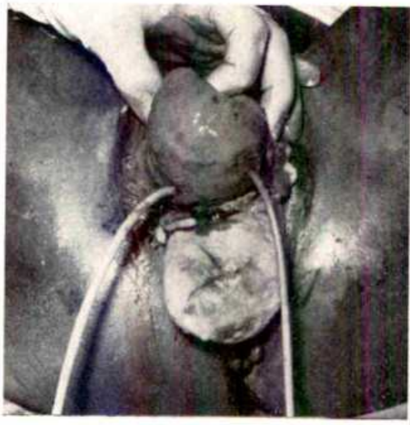

FIG. 1

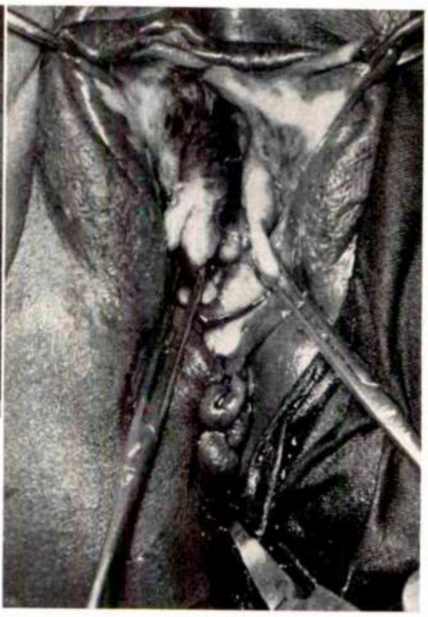

FIG. 2

Fig. 1.—Transurethral invasion of the bladder.

Fig. 2.—Partial urethral destruction associated with gross dilatation.

Six weeks post-operatively a careful assessment was made under anæsthesia. The urethra was still patulous and was estimated to be only 2 cm. long. The 2 posterior tags at the urethral opening remained. There were prominent cystocele and rectocele and although there was now no uterine descent the cervix remained abnormally long. It was decided to do an anterior colporrhaphy, amputation of cervix and posterior colpoperineorrhaphy. The posterior urethral tags were used to elongate the urethra, which was also buttressed.

Post-operatively the urethral repair healed well and full continence returned. The urine was clear and the bladder residue was minimal.

The patient was discharged home having spent nearly 3 months in hospital.

DISCUSSION

Inversion of the bladder is rare and usually occurs in the newborn, in children or in young women. Heyns, who collected 40 cases from the literature up to 1941, found that the inversion usually occurred slowly and was often associated with coughing or some other form of straining.

Klauser (1922) described four types of inversion of the bladder, although not much of the pathophysiology was known at the time. Classification is still open to doubt and needs modernising according to recent reports, but more important is some consideration of causes. The authors have attempted a revision of the classification as follows:

(a) *Urethral mucosal prolapse*: This happens especially in infants with cystitis. In infants the base of the bladder is conical rather than flat and urethral mucosal sliding occurs easily.

(b) *Prolapse of polyphoid lesion in bladder*: Papilloma; sarcoma botryoides.

(c) *Partial or complete inversion*: with pre-existing abnormalities such as pregnancy, vesicovaginal fistula, short urethra and procidentia.

In adults, the bladder base is normally flat but can be distorted or weakened especially by gross prolapse. In those cases with large vesico-vaginal fistulae (Mahfouz, 1938; Moir, 1961; Lawson, 1967) partial prolapse is common but self-reducing. Inversion down the urethra requires some basic urethral weakness or abnormality.

It has been shown that bladders contract as in Figure 3 (Kjellberg *et al.*, 1957; Emmett, 1964). It is obviously those that contract as in Figure 3B which would be more likely to prolapse. Figure 3B shows the posterior wall lying flat over the internal meatus. If the bladder base becomes conical (as in infancy and possibly with utero-vaginal prolapse) it could let the posterior wall prolapse, and once the posterior wall had entered and been gripped by the urethra it would enlarge and become œdematous, and then be extruded either by pressure or muscular contraction or both. Spontaneous reduction due to bladder filling is probably the reason why the condition does not occur more commonly; but once it is firmly gripped by the urethra (and in our case with a basically short urethra protrusion probably occurred to the external meatus early on) reduction may be impossible. Anuria would follow and the inversion would proceed. Our opinion is that the combination of ligamentous laxity and the short urethra in our case combined to produce an irreversible situation.

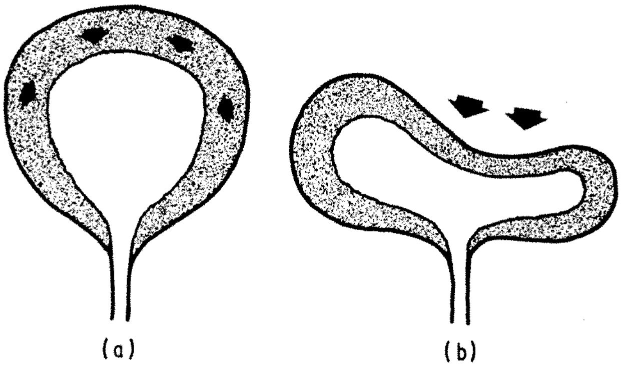

FIG. 3
The mechanism of bladder contraction.

The other predisposing lesion in this case may have been the rectal stricture. Defæcation would have required considerable straining and the diarrhœa before prolapse was probably spurious " overflow " with fæcal impaction.

Three cases of acute inversion of the bladder occurring during or immediately after delivery have been described by Heyns (1941), Mahfouz (1938), and Sutherland and Merki (1964). All these were treated by direct transurethral reduction and in all 3 the urethra and its sphincters were torn. The authors claim that 2 were definitely torn at the time of reduction and in one case it is not stated when the tear occurred. On the other hand it is possible that the sphincters were torn during delivery and that prolapse occurred through ruptured urethra. Uterine contractions and bearing down are presumably precipitating factors acting on a lax and toneless bladder wall, but this is an insufficient explanation since the condition is so rare in labour.

St George (1970) describes a case of spontaneous complete transurethral inversion of the bladder in a post-menopausal woman. His explanation of the case is that as a result of a fall part of the bladder wall was gripped by the internal urethral sphincter, then the increased intra-abdominal pressure due to the pain caused the prolapse to progress until the bladder became completely inverted. The inversion was reduced through the urethra without damaging it. It is difficult to see how the fall had anything to do with the subsequent events in this case, and though St George (1970) claims that the urethra was not damaged during reduction, an accurate description of the appearances after reduction is not given.

In the case reported here there were 2 pre-existing lesions, the procidentia which presumably damaged the supporting ligaments and the urethral defect from the previous lymphogranuloma venereum (not proven). Though the internal meatus was apparently functionally intact, it is likely that the lax supporting ligaments allowed the bladder base to become conical during voiding and that the dome of the bladder was poorly supported by the urachus. During the few days prior to complete prolapse the difficulty in voiding was probably due to invagination of the bladder dome down the urethra. Straining probably completed the inversion. The urethral tags were fully epithelialised and must therefore have existed before the prolapse.

From our experience with this case it would seem reasonable to disregard repairing the urethral incision until a later date. When the surrounding œdema has subsided and the urethral dilatation has recovered, a better assessment can be made. We agree with St George (1970) that every case of inversion of the bladder has to be treated on its own merits. Further surgery would be indicated for incontinence or prevention of recurrence. Repair of lax supporting ligaments and fixation of the dome to anterior abdominal wall would seem the best method of preventing recurrence.

SUMMARY

1. A case of complete acute transurethral inversion of the bladder associated with procidentia is reported. The management is outlined.
2. A classification of the types of inversion of the bladder and their corresponding precipitating factors is attempted.
3. A review of the literature is given.

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CONTINENCE AFTER SCROTAL FLAP URETHROPLASTY?

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Scrotal flap urethroplasty is a safe and effective technique for treating long urethral strictures involving the bulbar and prostatic urethra (Blandy *et al.*, 1968, 1971). In this procedure, as in the comparable methods of Bengt Johanson (1953), Wells (1967), Williams (1968), Leadbetter (1960), Gil-Vernet (1966), and Turner-Warwick (1968), a full thickness flap of scrotal skin is let in to the divided posterior urethra. In dividing the posterior urethra, which is often surrounded by very dense fibrous tissue, we must have severed the external urethral sphincter. None of 70 patients has been incontinent of urine afterwards (Blandy *et al.*, 1971).

Table I

Name	Age at Operation	Length of Dilatation Before Urethroplasty	Cause of Stricture	Position of Stricture	Previous Prostatectomy	Fully Continent
W. T.	44	24 years	Fractured pelvis Ruptured urethra	Membranous urethra	No	Yes
J. W.	56	8 years	Post-gonococcal	Bulb	Retropubic	Yes
B. N.	59	16 years	Poor stream since age 30 Not apparent	Bulb	No	Yes
C. S.	35	14 years	Fractured pelvis Ruptured urethra	Membranous urethra	No	Yes
S. B.	56	34 years	Fell astride	Bulb	No	Yes
J. R.	51	20 years	Post-gonococcal	Bulb	No	Yes
P. S.	59	36 years	Post-gonococcal	Bubl	No	Yes
T. M.	22	Nil	Not apparent Kicked in perineum age 14	Bulb	No	Yes
B. A.	61	1 year	Post-prostatectomy	Bulb	Retropubic	Yes
W. W.	52	16 years	Post-instrumentation	Bulb	T.U.R.	Yes
H. M.	83	30+ years	Not apparent	Membrane	T.U.R.	Slight dribble

We found it difficult to understand why patients who had scrotal flap urethroplasty were not incontinent. It is more difficult to understand those cases in whom prostatectomy has been performed in addition to scrotal flap urethroplasty. One might expect that in such patients both internal and external sphincters would be divided, and that incontinence must be inevitable. In practice not one of 9 patients has had any want of control. We therefore set out to investigate these patients, to see if we could localise the zone in which a sphincter was situated, and to see how it compared with the sphincter mechanism of men who had undergone neither prostatectomy nor urethroplasty.

Method.—Seven normal patients were studied, and 11 patients who had had urethroplasties. Of these 11 patients, 4 had been subjected to prostatectomy. The case details are shown in Table I.

The technique used for measuring the urethral pressure profile was that of Brown and Wickham (1969), modified by Harrison and Constable (1970), but using a miniature Holter pump (series No. RL 175) in place of the motor-driven syringe (Edwards, 1971). A constant flow rate of 2 ml. per minute was used for all the observations.

TABLE II

Control Series

Patient	Length (cm.)	Urethral Pressure (cm. H_2O)								
1	5·6	...	10	20	24	24	**52**	22	...	...
2	5·4	...	12	28	28	40	**50**	48	...	...
3	5·8	...	...	10	12	44	**62**	34	22	...
4	5·2	...	20	20	22	44	**46**	32	...	...
5	6·4	...	12	16	12	38	**46**	38	30	...
6	7·2	10	20	20	20	50	**74**	40	20	...
7	8·2	16	32	48	48	50	**74**	60	40	20
Mean	6·4	13	19	23	24	41	**56**	39	20	20

Sphincter pressure shown by bold figures

TABLE III

First-stage Urethroplasty—Rest

Patient	Length (cm.)	Urethral Pressure (cm. H_2O)											
M.	7·8	...	...	26	24	40	60	**88**	50	40	20	...	...
A.	9·0	...	20	28	30	36	44	**46**	34	20	10	...	...
R.	12·0	10	15	15	15	15	16	**20**	14	14	10	10	5
T.	4·8	...	...	...	4	18	18	**20**	16	...	...	...	...
B.	5·4	...	...	10	18	20	20	**32**	20	...	...	...	...
S.1	4·0	...	...	10	26	26	32	**48**	...	...	...	...	...
S.2	6·2	...	16	22	30	32	36	**40**	36	...	...	...	...
N.	8·4	...	10	20	30	32	42	**56**	20	18	20	10	...
W.1	7·0	...	4	6	12	14	40	**56**	34	12	4	6	...
W.2	4·3	...	...	...	...	...	22	**56**	25	22	...	...	...
Mean	6·9	10	15	17	21	28	33	**46**	28	21	13	9	5

Sphincter pressure shown by bold figures

Urethral pressure profiles were measured with the patient in the semi-lithotomy position. Local anæsthesia of the urethra was achieved with lignocaine and chlorhexidine gel—it has been found that the use of local anæsthetic agents does not influence the urethral pressure profile results (Edwards, 1970). Pressure profiles were measured at rest, until a series of reproducible profiles was obtained. When these control pressure profiles had been established, the patients were asked to contract their perineal muscles, as though to interrupt a urinary stream. Recording of the pressure profile during this period of squeeze gave the second series considered, that of " squeeze profiles ".

Results.—Seven normal male patients were assessed, and the results of the urethral pressure profile observations made in this group are shown in Table II. Figure 1 shows diagrammatically the correlation between the normal male lower urinary tract, and its function as expressed by the urethral pressure profile. An example of a normal male urethral pressure profile is shown

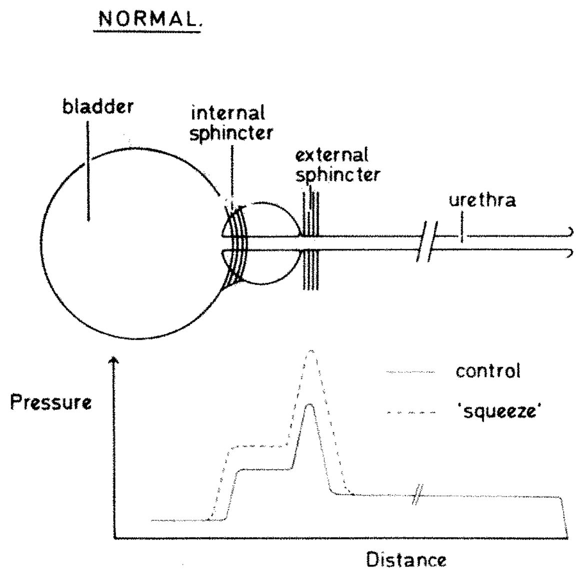

FIG. 1

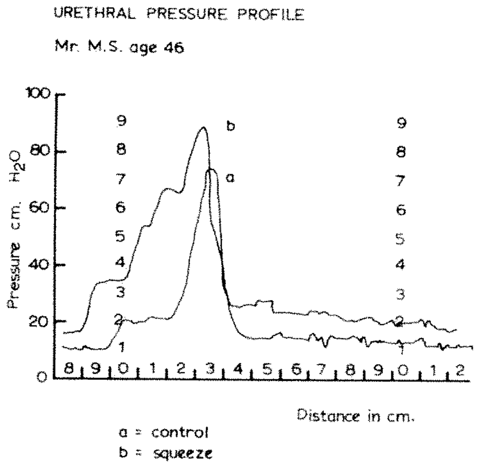

FIG. 2

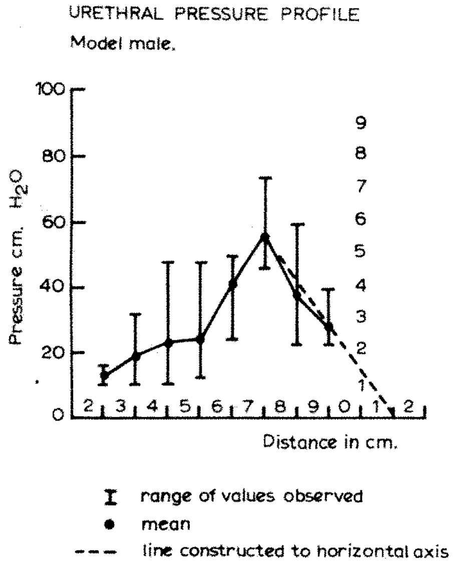

FIG. 3

Fig. 1.—The normal male urinary tract and its relation to the urethral pressure profile. The initial rise in pressure occurs at the bladder neck, and the second rise in pressure to a peak occurs at the external sphincter. The pressure at both these points is increased on " squeeze ".

Fig. 2.—A normal male urethral pressure profile.

Fig. 3.—The " model male " urethral pressure profile. Note the constructed line from the sphincter peak to the urethro-sphincteric junction, prolonged to meet the horizontal axis.

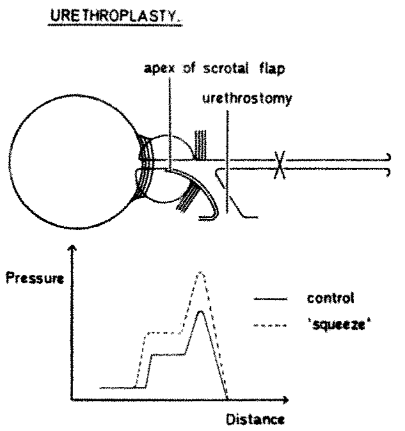

FIG. 4

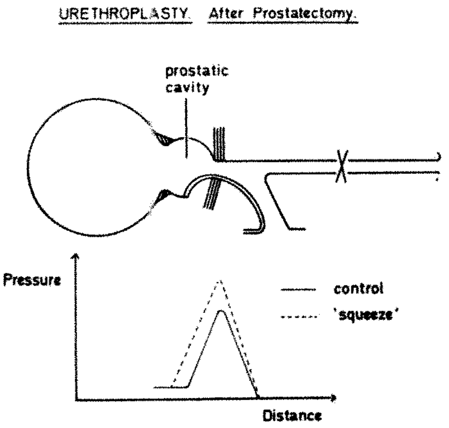

FIG. 5

Fig. 4.—The correlation between the lower urinary tract following first-stage urethroplasty and the urethral pressure profile. The long plateau of anterior urethral pressure is no longer present.

Fig. 5.—The correlation between the lower urinary tract following first-stage urethroplasty and prostatectomy, to the urethral pressure profile. The anterior urethral plateau is absent as in Figure 4. In addition, there is no longer an initial rise in pressure at the bladder neck, pressure rising smoothly to the external sphincter peak.

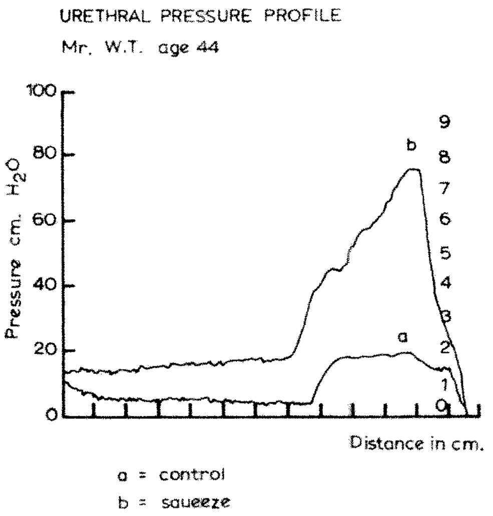

FIG. 6

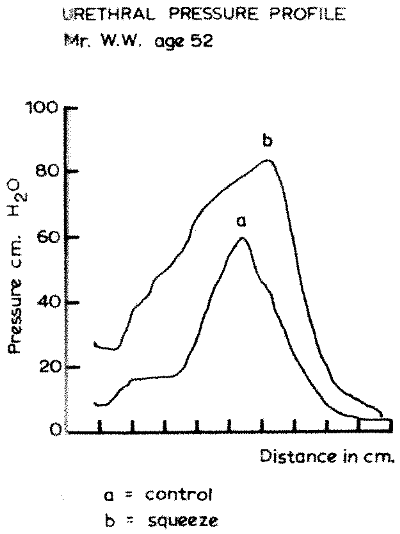

FIG. 7

Fig. 6.—Urethral pressure profile recording following first-stage urethroplasty.

Fig. 7.—Urethral pressure profile recording following first-stage urethroplasty and prostatectomy.

in Figure 2. A " model male " urethral pressure profile was calculated from the 7 profiles obtained and this " model profile " is illustrated in Figure 3.

The 11 patients with first-stage urethroplasties attended for assessment when the urethroplasty was considered to be satisfactory for closure. Table III shows the results of the pressure profile observations made in 10 first-stage urethroplasty cases at rest. Anatomy and function are illustrated in Figure 4, while Figure 5 illustrates the same principle when prostatectomy has been carried out in addition. Figure 6 shows an actual recording of an urethral pressure profile following urethroplasty, and Figure 7 shows the pressure profile of a patient after urethroplasty and prostatectomy. The results of the " squeeze " urethral pressure profiles measured in 9 urethroplasty patients are shown in Table IV. As before, composite profiles were constructed to represent those patients who had undergone first-stage urethroplasty: in the first instance considering the values obtained at rest, and then the values obtained on voluntary contraction of the pelvic floor. The composite profiles obtained in these two groups are illustrated respectively in Figures 8 and 9.

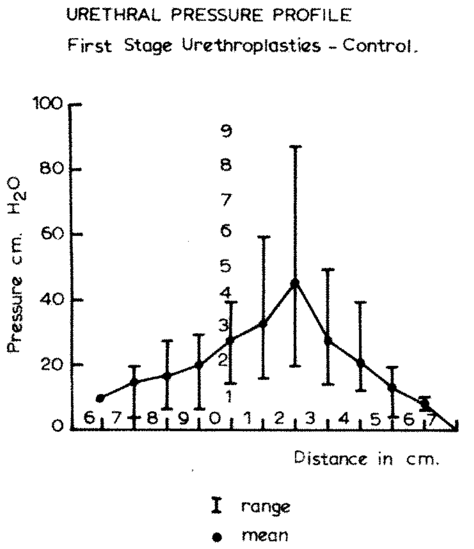

FIG. 8

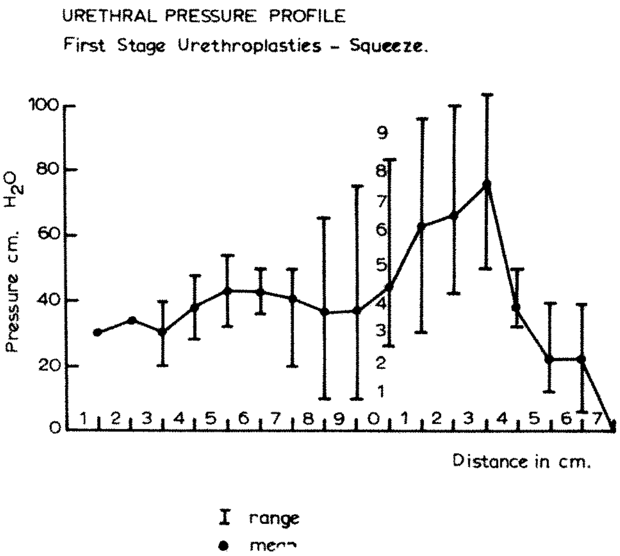

FIG. 9

Fig. 8.—Composite profile following first-stage urethroplasty.

Fig. 9.—Composite urethral pressure profile following first-stage urethroplasty and prostatectomy.

The external sphincter was defined as that level in the profile at which the profile pressure was maximum. The sphincter pressure in the control series, the first-stage series at rest, and the first-stage series on squeeze, were subjected to statistical analysis using Student's *t* test, as were the urethral lengths in the 3 groups. We found that there was no significant difference between the control profile amplitude at rest and the profile amplitude at rest following first-stage urethroplasty ($t = 0$). There was a significant difference between the control profile amplitude at rest and the first-stage amplitude on squeeze ($P < 0{\cdot}02, > 0{\cdot}01$), and between the first-stage amplitude at rest and the first-stage amplitude on squeeze ($P = 0{\cdot}05$) (Table V).

With respect to analysis of profile length, we defined, as the distal part of the external sphincter, that point on the urethral pressure profile at which the eyelets of the profile cannula emerged into the air. At that point, the profile was no longer curved, and became a straight, horizontal line. We constructed, on the normal profile diagram shown in Figure 3, a straight line from the sphincter peak to the urethro-sphincteric junction, and prolonged this straight line to meet the horizontal axis of the graph. This artificial construction allowed a direct comparison to be made between the profiles obtained in normal men, and those obtained in the men with perineal urethrostomies. When these lengths were subjected to statistical analysis, we were unable to demonstrate any significant difference between the 3 groups.

TABLE IV

First-stage Urethroplasty—Voluntary Contraction of the Perineum

Patient	Length (cm.)	Urethral Pressure (cm. H_2O)															
A.	13·0	...	...	20	28	32	36	40	44	48	48	50	50	**50**	44	30	20
R.	14·0	30	34	40	48	54	50	50	54	58	60	66	68	**74**	50	18	...
T.	5·6	...	...	...	...	...	...	...	...	18	40	50	64	**78**	32	...	...
B.	6·2	...	...	...	...	...	...	...	10	20	26	30	84	**104**	40	...	...
S.1	5·2	...	...	...	...	...	...	...	...	10	26	28	42	**56**	38	...	...
S.2	7·6	...	...	...	...	...	36	50	66	76	84	96	100	**104**	36	...	...
N.	8·4	...	...	...	...	...	...	20	25	32	44	52	68	**76**	34	30	40
W.1	8·6	...	...	...	...	...	...	...	20	36	46	64	74	**80**	44	12	6
W.2	5·2	...	...	...	...	...	...	...	...	...	30	50	58	**60**	34	...	...
Mean	7·38	30	34	30	38	43	43	40	36	37	44	63	66	**76**	39	22	22

Sphincter pressure shown by bold figures

TABLE V

		SD	SE	$\bar{n}$	t	p
A.	C	12·5	4·74	56	...	...
	F	20	6·33	56	...	...
	S	19·1	6·3	76	...	...
	CF	...	7·86	...	0	...
	CS	...	7·8	...	2·84	0·02-0·01
	FS	...	8·9	...	2·25	0·05
L.	C	1·1	0·42	6·4	...	...
	F	1·83	0·58	6·9	...	...
	S	3·08	1·01	8·4	...	...
	CF	...	0·72	...	0·71	0·5
	CS	...	1·09	...	1·83	0·1
	FS	...	1·16	...	1·39	0·2

Where SD = Standard deviation.
SE = Standard error.
$\bar{n}$ = Mean observation.
A = Profile amplitude.
L = Profile length.
C = Control.
F = First-stage—rest.
S = First-stage—squeeze.
CF etc. = Standard of error of difference (C-F) etc.

DISCUSSION

We now have evidence that patients who have had a first-stage urethroplasty are still able to squeeze and compress their urethræ, and hence they are continent.

What has happened to the sphincter mechanism following urethroplasty? It may be that the sphincter has been severed, but re-joined; or that the sphincter has been pushed back and not really severed at all.

Three urethral closure mechanisms are believed to operate as a sphincter unit, and these three mechanisms are the intrinsic urethral musculature, the internal sphincter, and the external sphincter. The last two are the " passive " and " active " sphincters respectively of Caine and Edwards (1958), but for the purpose of the present discussion we would prefer to use the terms involuntary and voluntary sphincters.

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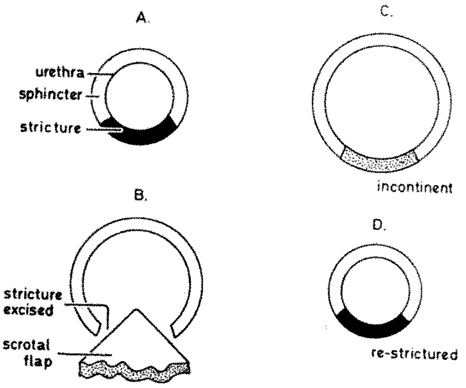

FIG. 10

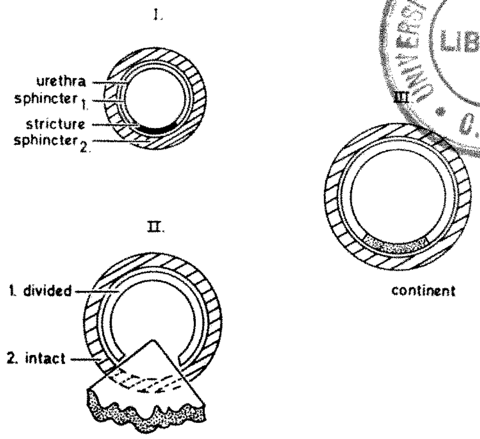

FIG. 11

Fig. 10.—Diagram illustrating the previous concept of sphincter function following urethroplasty.

Fig. 11.—Diagram illustrating the current concept of sphincter function following urethroplasty.

Following prostatectomy the internal sphincter has been ablated, and continence must depend on the external sphincter and the intrinsic urethral musculature. It has been stated that the external sphincter is incapable of maintaining continence at rest (Turner-Warwick and Worth, 1970), but we must disagree with this observation in the light of the evidence here presented. If continence after prostatectomy depends on the intrinsic urethral musculature, then how can we explain continence after urethroplasty when this internal urethral mechanism has been severed? A stricture must be an integral part of such a mechanism as shown in Figure 10, A. Excision of this stricture, and its replacement by a scrotal flap (Fig. 10, B) must result in an incompetent sphincter (Fig. 10, C) since no sphincter could contain urine unless it formed a complete ring. If this hypothesis were true, continence could only result if fibrosis of the scrotal flap occurred, the sphincter ring was reconstituted, and stricture re-developed (Fig. 10, D). This does not happen: the prime features of the scrotal flap procedure for urethral stricture are that re-stenosis does not occur, and that the patients are completely continent.

We would suggest that following prostatectomy, the nature of the voluntary external sphincter changes. We think that after prostatectomy, the voluntary external sphincter adopts an " involuntary " role, and that the new role of this sphincter in the maintenance of continence is more important than any part played by the intrinsic urethral musculature. We may consider the external sphincter as a composite unit in which both voluntary and involuntary components are present. Stricture involves the involuntary part of this unit (Fig. 11, I), and it is this involuntary unit that is resected with the stricture, and a scrotal flap inserted into the defect so created (Fig. 11, II). Since at this stage the stricture has been successfully removed, and continence has been maintained (Fig. 11, III), it follows that the voluntary sphincter has once more adapted itself to play an involuntary role.

We conclude that following urethroplasty, continence is maintained by the external sphincter. This sphincter is capable of maintaining continence at rest, as it adopts its involuntary role, and that at times of stress it reinforces itself voluntarily to maintain continence against the increased forces which are tending to produce incontinence. In short, the external sphincter is the key to continence following urethroplasty, and it is the adaptability of this muscle that is responsible for the maintenance of continence.

SUMMARY

1. In order to localise the zone at which the urethral sphincter is situated in men we investigated 7 normal patients, 7 patients who had had urethroplasties only, and 4 who had had both urethroplasty and prostatectomy.

2. We found that all these patients were continent.

3. Continence after urethroplasty and prostatectomy depends upon the external sphincter which, under these conditions, is capable of preserving continence at rest, that is, of taking up a new " passive " role in the absence of an internal sphincter and an intact intrinsic urethral musculature.

We would like to thank Professor J. P. Blandy for allowing us to study patients under his care, and for his continued encouragement and advice.

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A CYSTOMETROGRAPHIC STUDY TO ASSESS THE INFLUENCE OF ATROPINE, PROPANTHELINE AND MEBEVERINE ON THE SMOOTH MUSCLE OF THE BLADDER

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AFTER Heidenhain and Colberg first used the cystometer in 1858 to measure the tone and contractions of the vesical detrusor muscle, 70 years passed until Rose and Deakin (1928) introduced the cystometrogram to study the pharmacology of the bladder. It is only in the last 2 decades that the cystosphincterogram has been developed as a useful addition to the armamentarium available to evaluate the reactions of the bladder to different drugs. Lapides (1958) studied the effect of adrenergic, adrenolytic and antihistaminic compounds and found them to have no effect on the bladder, while cholinergic drugs, such as urecholine or neostigmine, accentuate the motor impulses on the m. detrusor, thus causing increased voiding contractions. It is generally known that anticholinergic drugs, such as propantheline and hyoscine butylbromide, can cause a considerable reduction of the contractility of the detrusor muscle, and thus may provoke a total urinary retention in patients suffering from benign prostatic hypertrophy. Surprisingly, atropine —the most potent anticholinergic compound—was found to have very little influence on bladder tone and contractility (Ambache, 1955).

As spasmolytics are widely prescribed at present for the treatment of spastic conditions, especially those affecting the gastro-intestinal tract, we thought it would be useful to compare the effects of some spasmolytic drugs on the bladder by means of cystometrography.

The drugs studied were atropine, propantheline and meberverine.

Atropine is mainly used in surgical pre-medication, because of its effectiveness to reduce salivary secretion.

Propantheline is known to be useful in relieving the pain associated with duodenal ulcers, although it has little influence on the actual healing of peptic ulcers. There is evidence that the drug is useful in the management of the neurogenic uninhibited bladder and the neurogenic automatic bladder (Kohler and Morales, 1968).

Mebeverine is a spasmolytic drug, acting directly on the smooth muscle and with no known anticholinergic side-effects in therapeutic doses. Its pharmacological properties were described by Lindner *et al.* (1963) and by Connell (1965), who showed that 50 mg. mebeverine i.v. gave a strong reduction of colonic motility, lasting approximately 20 minutes. In a placebo-controlled, double-blind study, Connell (1965) also showed mebeverine to be effective in the irritable colon syndrome.

Materials and Methods.—For the cystometrography we used the apparatus of Lewis (1939) and the method applied was the same as that described by Baumann (1955), Grasset (1961) and Bauer (1963).

In all subjects readings were done 15 minutes and 45 minutes after injection of the drugs. Tone of the empty bladder, sensation (first desire to void, sensation of bladder fullness and bladder capacity), motility (bladder contractions, micturition pressure) were recorded, as well as the pressures of the internal and external vesical sphincters. The studies were performed in 22 patients, 6 of whom had normal bladders, no enlargement of the prostate and no residual urine. The other 16 suffering from varying degrees of prostatic enlargement (mostly benign prostatic hypertrophy) or some other micturition impediment, some of them with indwelling catheter after total urinary retention. Two patients (cases No. 11 and No. 12) showed besides the " benign pro-

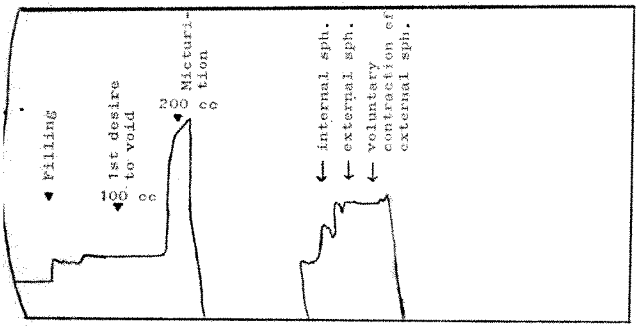

FIG. 1 Case 16. Basic values.

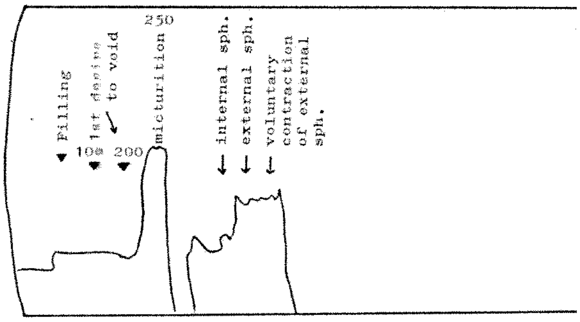

FIG. 2 Case 16. Forty-five minutes after 100 mg. mebeverine

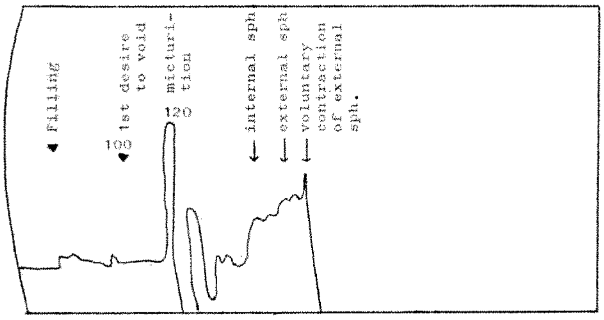

FIG. 3 Case 16. Forty-five minutes after 0·5 mg. atropine.

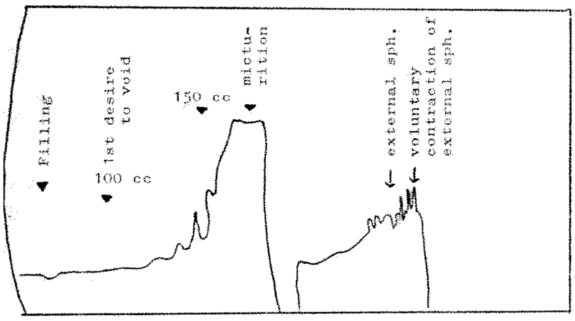

FIG. 4 Case 2. Basic values.

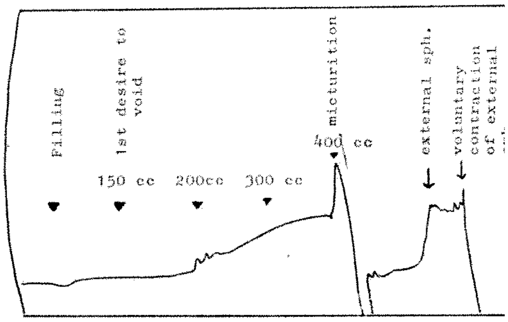

FIG. 5 Case 2. Forty-five minutes after injection c
30 mg. propantheline.

static hypertrophy " also signs of neurogenic bladder dysfunction. 16 patients (cases No. 1 to No. 16) received 100 mg. mebeverine i.m. and 0·5 mg. atropine i.m. the following day. Six patients received only propantheline 30 mg. i.m.

Results.—The results are given in Tables I and II.

In none of the patients were there changes of the tone of the empty bladder, sphincteric pressures or sensation and therefore these observations were omitted from the tables.

The bladder capacity and micturition pressure values for mebeverine and atropine 15 minutes and 45 minutes after injection, showed no significant differences from the pre-injection values, for propantheline the drug effect was most pronounced after 45 minutes.

Tables I and II give only the values for bladder capacity and micturition pressure 45 minutes after the injection of each compound. From Table I it is obvious that neither atropine 0·5 mg. i.m. nor mebeverine 100 mg. i.m. (a frequently used dose in surgical pre-medication) has an effect on bladder capacity or micturition pressure. Propantheline 30 mg. i.m., however, abolished the micturition reflex completely in 5 out of 6 patients and also resulted in a considerable increase in bladder capacity in 5 out of the 6 patients.

DISCUSSION

Pharmacology of the bladder is an important but largely unexplored field. Spasmolytic drugs are of interest to the urologist for 2 reasons. Firstly in a positive sense because they may have a beneficial effect on the management of the patient with a neurogenic uninhibited bladder. Here the anticholinergic drugs, like propantheline or hyoscyamine may be very valuable, although their usefulness is hampered by their side-effects. Another drug which may prove to be useful in these conditions is diazepam (Schmidt, 1965; Roussan *et al.*, 1967). The second area where spasmolytic drugs are important to the urologist is in patients with biliary and renal colics. Indirectly the urologist may be involved when spasmolytics are used in other fields of medicine. The use of spasmolytics is becoming more and more popular in the gastro-intestinal motility disorders, of which the irritable colon syndrome probably is the most frequent. If these drugs are given to elderly male patients, it is important to realise that the risk of inducing iatrogenic micturition problems may arise if the drug prescribed can adversely influence micturition capability in these individuals. In particular in patients with prostatic hypertrophy or other urinary flow impediments in the lower urinary tract the use of anticholinergics can lead to complete urinary retention.

Our own study gives evidence that neither atropine nor mebeverine in the normally used doses influences micturition pressure or bladder capacity. For atropine, this is consistent with the findings of Ambache (1955). Propantheline (in the recommended therapeutic dose) and other similar synthetic anticholinergics (Lapides and Dodson, 1953; Kohler and Morales, 1968) can cause an increase in bladder capacity together with a decrease in micturition pressure, which may lead to urinary retention in subjects with prostatic enlargement. In patients suffering from prostatic enlargement, for whom treatment with spasmolytics is desired, propantheline and other synthetic anticholinergics should be considered contra-indicated, whereas mebeverine and atropine can be given safely.

SUMMARY

In 22 subjects the effect of atropine 0·5 mg. i.m., mebeverine 100 mg. i.m. and propantheline 30 mg. i.m. on bladder capacity, micturition pressure and other aspects of bladder motor function, was compared.

Atropine and mebeverine were found to have no effect on the bladder function, whereas propantheline increased bladder capacity and decreased micturition pressure, thus causing total urinary retention in 5 out of 6 patients with prostatic enlargement receiving this drug.

TABLE I—Changes of Bladder Capacity and Micturition Pressure 45 minutes after administration of 100 mg. Mebeverine i.m. and after 0·5 mg. Atropine i.m.

Case No.	Record No.	Birthdate	Basic Values		After Mebeverine		After Atropine		Remarks
			Capac. (cc.)	Mict. Press. (mm. Hg.)	Capac. (cc.)	Mict. Press. (mm. Hg.)	Capac. (cc.)	Mict. Press. (mm. Hg.)	
1	449/68	5.7.36	800	90	600	90	550	90	1968: kidney stone, pyelo-lithotomy on left side
2	489/68	9.8.24	400	60	200	60	300	60	1951: uretero-lithotomy 1967: gallstone, verified by cholecystography. No operation
3	518/68	4.6.22	500	...	450	...	450	...	1959: compression fractures of D_3 1966: compression fracture of D_{10-11}
4	513/68	29.10.45	300	...	300	...	250	...	Upper urinary-tract infection (*E. coli*), following ureter colic L.
5	546/68	30.1.06	550	...	520	...	320	...	Under 2 mg. valium t.i.d.
6	148/68	24.9.99	380	64	250	62	220	60	1968: nephro-ureterectomy for papillomas
7	378/68	11.11.18	220	...	150	...	150	...	1920: poliomyelitis, paralysis of left LE
8	476/68	10.2.85	200	60	150	64	*400*	34	BPH and bladder stone
9	570/68	16.3.90	300	...	350	...	350	...	Indwelling catheter, ca of prostate
10	595/68	27.5.91	350	75	350	70	250	70	BPH
11	599/68	18.8.10	120	95	100	150	100	102	1941: gun shell injury of pelvis—bladder dysfunction 1944: gun shell injury of skull *now: neurogenic uninhibited bladder*
12	619/68	1.9.92	100	90	80	78	30	78	1945: compression fracture of L_1 *now: neurogenic uninhibited bladder*
13	612/68	29.5.98	200	140	120	108	40	92	Indwelling catheter for 3 weeks
14	665/68	28.11.00	200	90	50	98	180	74	1968: transvesical prostatectomy for BPH
15	652/68	29.9.98	300	40	250	...	200	...	1956: cerebral vascular accident with following hemiparesis left side
16	700/68	19.3.04	300	75	250	82	120	94	Mild BPH, nephrolithiasis L. No operation

TABLE II—Changes of Bladder Capacity and Micturition Pressure 45 minutes after Administration of 30 mg. Propantheline

Case No.	Record No.	Birthdate	Basic Value		After Propantheline	
			Capac. (cc.)	Mict. Press. (mm. Hg.)	Capac. (cc.)	Mict. Press. (mm. Hg.)
17	405/69	3.10.90	350	60	500	64
18	401/69	19.9.91	150	100	400	No mict.
19	Out-patient	27.4.17	400	50	400	No mict. Irritable bladder in climax
20	442/69	13.9.38	400	114	600	No mict. Hypertroph. of int. ves. sph.
21	370/69	30.7.84	100	55	350	No mict.
22	428/69	29.7.99	500	68	650	No mict.

It is concluded that propantheline and other similar synthetic anticholinergics are contraindicated in patients with prostatic enlargement, but that atropine and mebeverine in the mentioned doses are not.

Proprietary Names:

mebeverine = Duspatalin, Colofac
propantheline = Probanthine
hyoscine butylbromide = Buscopan
diazepam = Valium

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PYELO-ILEOSTOMY AND PYELO-ILEO-CYSTOSTOMY

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HYDRONEPHROSIS due to obstruction or atony of the ureter in patients with a single kidney or bilateral renal disease always poses a difficult and as yet controversial therapeutic problem.

In the cases dealt with hereunder, the damage to the upper urinary outflow tract was irreversible, although the kidney itself could still function normally provided that the obstruction was relieved by an efficient drainage procedure.

Among the various conditions for which ileal replacement or bypass of the ureter has been used are:

(1) Irreversible hydronephro-ureter (King and Scott, 1964; Skoglund and Ansell, 1968).

(2) Ureteral strictures, inflammatory, traumatic and post-irradiation (Creevy, 1965; Weinberg, 1970).

(3) Intractible calculous obstruction (Goodwin *et al.*, 1959, 1961).

In 2 cases of hydronephrosis with nephrolithiasis and severe ureteral obstruction, treated in our department, a bypass drainage procedure was done using an isolated ileal loop in order to conserve the remaining renal tissue while avoiding the complications frequently encountered following permanent nephrotomy. A third patient who underwent pyelo-ileo-cystostomy elsewhere has been under our observation for the last 8 years.

CASE REPORTS

Case 1.—A woman, aged 32 years, who had undergone right nephrectomy elsewhere in 1956 for nephrolithiasis. She was first admitted to our hospital in 1964 with severe oliguria, uræmia, hæmaturia and urinary tract infection. An attempt at ureteric catheterisation failed due to obstruction at the lower end of the left ureter. Plain abdominal X-ray revealed a number of calculi in the region of the left kidney and ureter.

Following left emergency nephrostomy, fluid and electrolyte replacement and antibiotic therapy, there was marked improvement, renal function returning to normal. Further X-ray investigation showed gross hydronephrosis, multiple ureteral strictures and calculi in the kidney and ureter (Fig. 1). At operation, 2 months later, a number of calculi were removed from the renal pelvis and upper ureter, and a pyelo-ileo-cutaneous anastomosis was performed, using an ileal conduit approximately 25 cm. in length.

One month later, following pyelographic confirmation of satisfactory drainage via the pyelo-ileostomy, the nephrostomy tube was removed. During the ensuing 4 years her general condition remained satisfactory, repeat X-ray examinations showing a marked decrease in the degree of hydronephrosis (Fig. 2). Most of her urine was passed through the ileostomy. Renal function tests and serum electrolytes were consistently normal. During the early part of this period a number of calculi were passed spontaneously through the ileostomy. There were no overt urinary infections although on routine periodic urine examinations *E. coli* was occasionally cultured. Following administration of Nitrofurantoin, the cultures reverted to sterile.

In 1968, after being completely asymptomatic during the latter few years and following her continual insistance on having the ileostomy " closed ", the patient underwent re-operation. The cutaneous ileostomy was detached and the distal end of the conduit was anastomosed to the bladder, thus converting the ureteral bypass into a pyelo-ileo-cystostomy. At the same operation the remaining stone was removed from the lower part of the ureter. Since then (3 years) the patient has felt well and passes urine normally. There has been no deterioration in her renal function, serum electrolytes and pyelographic appearance of the kidney. There is minimal reflux into the lower part of the ileal conduit and there have been no further infections.

Case 2.—A woman, aged 37 years, underwent operations in 1967 for calculi in the lower ends of both ureters and a staghorn calculus in the left kidney (Fig. 3). In 1968 she was admitted with a poorly functioning, grossly hydronephrotic right kidney, recurrent right ureterolithiasis at the lower end and a recurrent staghorn calculus of the left kidney. At operation a number of small stones were removed from the right renal pelvis. The upper end of the right ureter showed severe fibrous stricture. Right renal bypass drainage was affected this time by a 35 cm. long ileal conduit, the upper end of which was anastomosed to the renal pelvis, the lower end being brought out as a cutaneous ileostomy. About 10 cm. proximal to its lower end, the conduit was anastomosed to the bladder, side-to-side, thus forming a pyelo-ileo-cysto-cutaneous anastomosis (Figs. 4 and 5). During the subsequent 2 years the patient felt well and passed most of her urine per urethram. While the ileostomy served as a " pressure valve " and made possible retrograde X-ray studies of the pyelo-ileo-cystostomy, the patient did not need to use an ileostomy bag, a light dressing sufficing. I.V.P. showed improvement in the function of the right kidney. Serum electrolytes, blood urea, creatinine and clearance tests were within normal limits.

FIG. 1

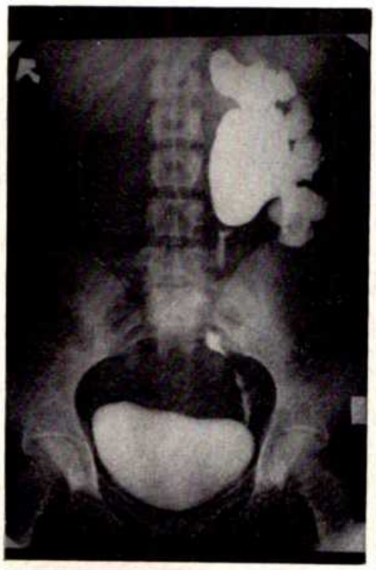
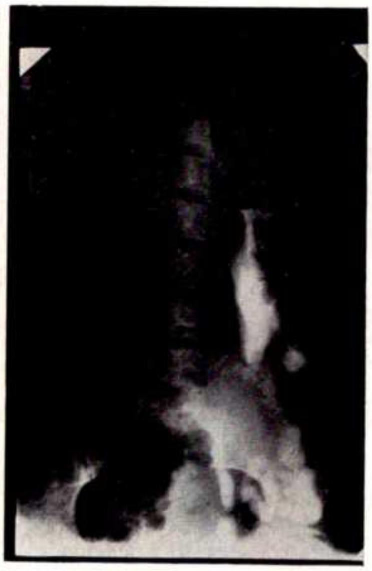


FIG. 2



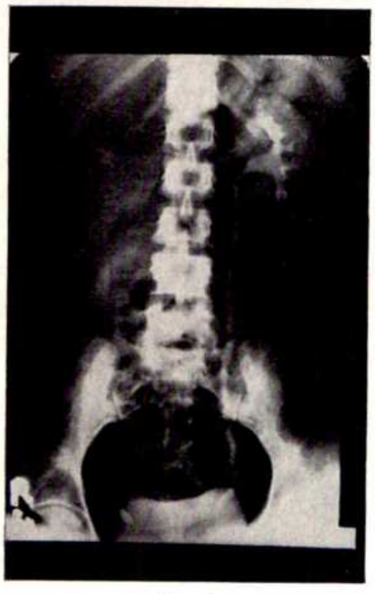


FIG. 3

Fig. 1.—Case 1. Pre-operative pyelogram (filling via nephrostomy): hydronephrosis, nephrolithiasis, multiple ureteral strictures

Fig. 2.—Case 1. Retrograde ileo-pyelogram (filled via ileostomy): marked reduction of hydronephrosis.

Fig. 3.—Case 2. Severely hydronephrotic, poorly functioning right kidney. Calculus near lower end of ureter: non-opaque staghorn calculus in the left renal pelvis.

This patient, too, insisted repeatedly on having her ileostomy closed. Six months ago, the terminal part of the ileal conduit was excised, leaving a pyelo-ileo-cystostomy which has since functioned well. I.V.P. shows no further deterioration, blood chemistry has remained normal, urine cultures are sterile, and the patient micturates normally.

Case 3.—A woman, now aged 42, underwent bilateral pyelo-ureteroplasty 11 years ago. Her left kidney has since remained non-functioning. Nine years ago she underwent right pyelo-lieo-cystostomy. Since coming to this country 8 years ago, she has been under our care and we have thus had the opportunity to observe her maintenance of good renal function, normal serum electrolytes and lack of urinary infection.

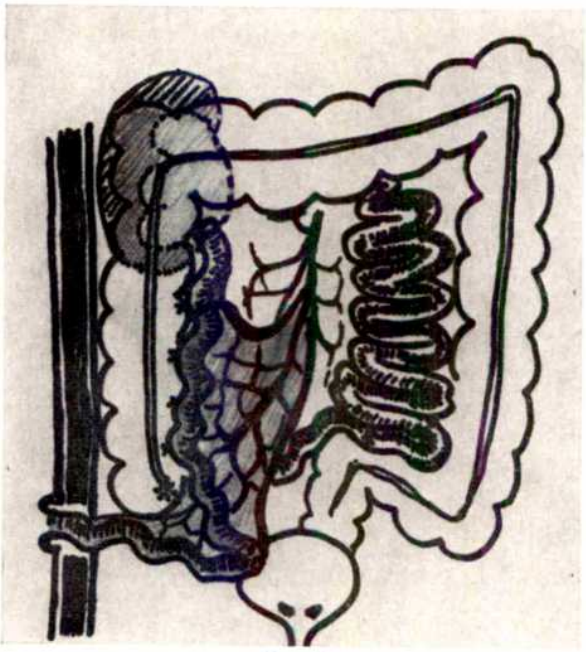


FIG. 4

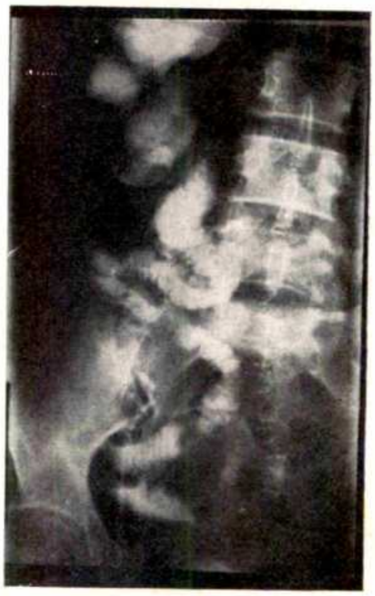


FIG. 5

Fig. 4.—Case 2. Pyelo-ileo-cutaneous anastomosis with side-to-side ileo-cystostomy (pyelo-ileo-cysto-cutaneostomy).
Fig. 5.—Retrograde pyelo-ileogram.

DISCUSSION

Various authors have described complications following the use of an ileal conduit in the upper urinary tract and particularly after pyelo-ileo-cystostomy (Creevy, 1965).

(*a*) Failure of drainage from an atonic hydronephrotic renal pelvis in the face of a normally continent urethral sphincter (Fergusson, 1956).

(*b*) Electrolyte disturbance and hyperchloræmic acidosis due to reabsorption from the conduit.

(*c*) Progressive renal damage as a result of ascending infection, stasis, stone formation, mucous obstruction and reflux.

In our 3 cases we have as yet not encountered such complications. By first establishing free urinary drainage by means of cutaneous pyelo-ileostomy we have been able to observe the improved function of the previously obstructed kidney over a period of a few years. While we have not conducted pressure studies, image-intensifier-fluoroscopy has enabled us to evaluate renal pelvic tone and emptying ability through the ileal conduit, as well as vesical and sphincteric function. In our second case, in which pyelo-ileo-cysto-cutaneous anastomosis had been performed as the first stage, temporary occlusion of the cutaneous ileostomy enabled us to pre-test the efficiency of the ureteral bypass before deciding whether to excise the ileostomy. In the 2 cases operated on in our department, the ileal loop was placed isoperistaltically, although if this should endanger the vascular supply of the loop, it can function adequately when placed in an antiperistaltic direction, as was done in one of the cases described by Weinberg (1970). It should be noted that repeated examination of these 3 patients in our medical department revealed no metabolic calculogenic aetiology. Chemical analysis of the stones removed showed calcium and ammonium phosphate and calcium oxalate. Repeated examinations of the urine for tuberculosis and bilharzia were negative.

CONCLUSIONS

Drainage of the upper urinary tract by means of cutaneous pyelo-ileostomy is indicated in certain cases of irreparable upper ureteric strictures, severe atonic hydroureter and recurrent multiple renal calculi especially in the presence of bilateral renal disease or in the single kidney where permanent nephrostomy would otherwise be necessary.

In some of these cases it may be possible, the general condition and renal function permitting, to convert the pyelo-ileostomy at a later date into a pyelo-ileo-cystotomy. The latter procedure is simplified by performing a pyelo-ileo-cysto-cutaneostomy as the first stage, thus providing both free renal drainage and the possibility of pre-testing the efficiency of the ileal conduit as a ureteric bypass before finally excising the cutaneous ileostomy.

In the 3 cases described (2 of which had been previously managed by pyelo-ileostomy), the follow-up results of pyelo-ileo-cystostomy were satisfactory in respect of renal function, electrolyte balance and relative lack of infection.

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PARARENAL PSEUDOCYST

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Pararenal pseudocyst is an uncommon condition caused by renal trauma, in which there is an encysted collection of urine or serous fluid lying outside the renal pelvis and parenchyma. It has no epithelial lining and is limited by a false capsule derived from fibrosis of the surrounding tissues. In most reported cases it communicates with the collecting system by a tear in the calyces, pelvis or ureter. The term pararenal pseudocyst was popularised by Sauls and Nesbit (1962), but alternative names are pseudo-hydronephrosis, perinephric cyst and hydrocele renalis to indicate that sometimes the cyst surrounds the kidney.

Case Report.—A 69-year-old woman woke with sudden onset of left loin pain which radiated to the left groin. There were no urinary symptoms on micturition. Her blood pressure was 180/90 mm. Hg. There was a large tender mass in the left upper abdomen extending forwards from the loin.

There was no past history of renal disease, although she did sustain an injury to the left loin 4 years previously and was told she had fractured some ribs. Forty years before she had had an ectopic pregnancy and later that year had sanatorium treatment for pulmonary tuberculosis. Diverticular disease of the colon had ben diagnosed 8 years before.

The hæmoglobin was 13·1 g. per cent, white cell count 8,500 per c. mm. and the E.S.R. was 50 mm. in 1 hour. The plasma urea and electrolytes were normal. A midstream urine sample contained no cells and was sterile.

The intravenous pyelogram (Fig. 1) showed a large left kidney with poor function and dilatation of pelvis and calyces. The lower pole was displaced outwards by a mass which was faintly opacified by contrast material. The right kidney appeared normal.

A catheter was passed up the left ureter without difficulty, and 250 ml. of urine was aspirated, greatly reducing the size of the abdominal mass. The aspirate contained 100 red cells per h.p.f. and was sterile. The retrograde pyelogram (Fig. 2) showed appearances suggestive of a pararenal pseudocyst, although the radiologist could not exclude a tumour of the renal pelvis.

At operation, a large pseudocyst was found lying mainly posterior to the left renal pelvis but extending also in front of it so that the upper 2 cm. of the ureter were surrounded by cyst. The cyst communicated with the renal pelvis although because of some loculation it was not possible to identify the site of the original perforation precisely. The cyst wall was thick and fibrous and formed in part by necrotic fat. The mucosa of the renal pelvis appeared granular. The pseudocyst was excised and the opening in the renal pelvis closed using a polythene splint and a nephrostomy. The ureter was supported by buttressing the pernephric fat around it.

Post-operatively she made a good recovery and was discharged home 24 days later.

An intravenous pyelogram 3 months later (Fig. 3) showed satisfactory function on the left with only slight residual deformity of the pelvis and calyces.

Pathogenesis.—Based on etiology, Spriggs (1952) proposed a classification of perinephric cysts referring to cysts which more or less surround the kidney. Most follow perinephric extravasation of urine and are now called pararenal pseudocysts, but some follow resolution of a perinephric hæmatoma, and in still others it is not possible precisely to define the mode of origin, even after careful dissection.

The probable pathogenesis of pararenal pseudocysts has been fully discussed by Crabtree (1935), Pyrah and Smiddy (1953) and more recently by Sauls and Nesbit (1962). Following a tear in the renal pelvis or upper ureter, or a complete rupture of the renal substance into a calyx, urine escapes into the surrounding tissues. This is usually rapidly absorbed unless there is some ureteric obstruction either existing before the injury or caused by it as a result of pressure from the hæmatoma or later fibrosis. Such obstruction will allow urine to accumulate in the tissues where it excites an inflammatory response in the perinephric fat. Subsequent fibrosis forms a thick wall to the pseudocyst. It has no epithelial lining.

Experimentally, Delbet (1903) showed that a simple incision in the renal pelvis or ureter, without suturing, resulted in a small leakage of urine which was promptly absorbed. It is

FIG. 1

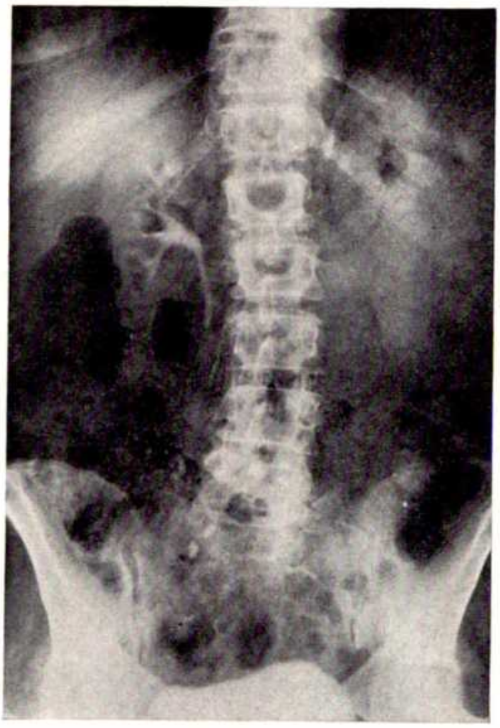
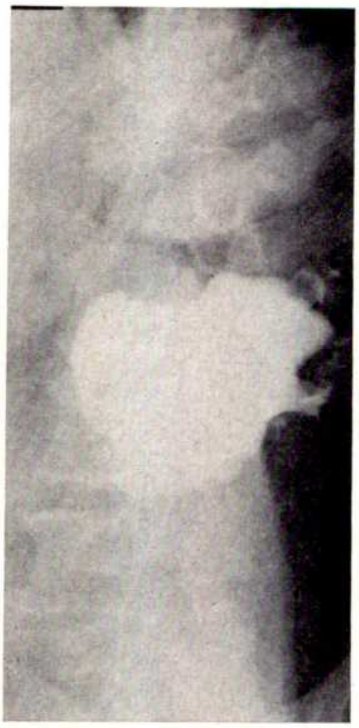


FIG. 2



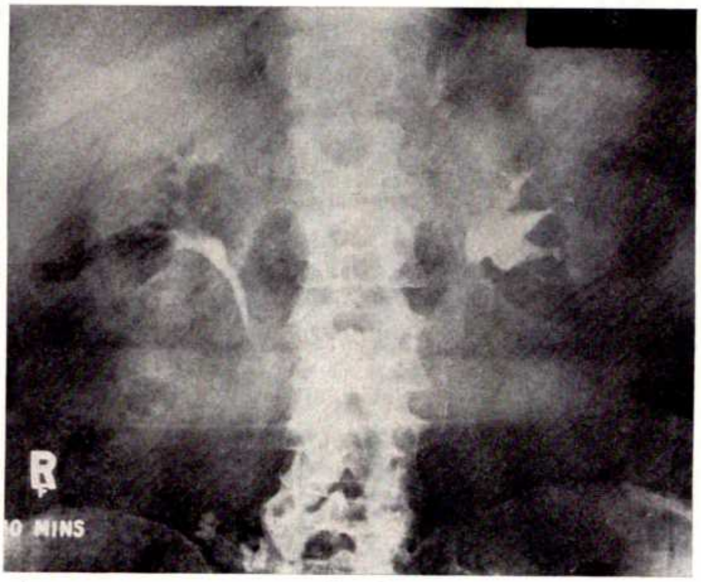


FIG. 3

Fig. 1.—Intravenous pyelogram shows large left kidney with poor function and dilated pelvis and calyces. The lower pole is displaced outwards by a mass faintly opacified by contrast material.

Fig. 2.—Retrograde pyelogram shows appearance suggestive of a pararenal pseudocyst confirms communication between dilated pelvis and the large irregular walled pararenal pseudocyst, which is displacing the lower pole of the kidney outwards.

Fig. 3.—Three months after operation: intravenous pyelogram shows satisfactory function on left with only slight residual deformity of pelvis and calyces.

common practice by some urologists to avoid suturing the ureter or pelvis after exploration to avoid stenosis, and no complications appear to follow this practice. Razzaboni (1922) was able to induce the condition in rabbits by dividing the pelvi-ureteric junction and simply re-approximating the perirenal tissues to the ureter.

DISCUSSION

The first case of pararenal pseudocyst was described by Hawkins in 1834, in a boy of 6 who was run over by a horse and cart. He died 10 days later and at autopsy 2 small holes were found in the renal pelvis leading into a large pseudocyst. In his review in 1935, Crabtree collected 20 cases from the literature and added 3 of his own. Nineteen cases have been reported since then and with this present case make a total of 43 cases which are here reviewed.

REVIEW OF 43 CASES

History of Trauma (Table I).—A history of trauma was obtained in 39/43 cases (90 per cent). Of these, 30 followed closed injury and 9 occurred post-operatively: 4 after pyelolithotomy, 2 after ureterolithotomy, 1 after a pyeloplasty and 2 after gynæcological procedures. The two latter cases were reported by Weintraub *et al.* (1964), but the pathogenesis is not clear from the case reports. In one, a woman of 41 years, there was a painful swelling in the right side of the abdomen, which developed 4 months after an abdominal hysterectomy and right salpingo-oophorectomy. The mass was incised and drained urine. However, the mass soon reappeared and at exploration a pseudocyst was found with the ureter lying completely severed at the pelvi-ureteric junction. Nephrectomy was performed. The second case, a 40-year-old woman, had had a difficult abdominal hysterectomy and bilateral salpingo-oophorectomy 4 months before for fibroids and a para-ovarian cyst. She presented with pain and an enlarging mass in the right flank. The lower ureter was identified by ascending ureterograms only as far as the pelvic brim. The pseudocyst was outlined after direct puncture. Nephrectomy was performed. Probably both these cases represent ureteric obstruction, but no definite cause for the rupture of the pelvis or ureter higher up, is stated.

TABLE I

History of Trauma

Trauma: Blunt		30
Operative: pyelolithotomy	4	
ureterolithotomy	2	
pyeloplasty	1	
gynæcological procedures	2	
		9
Total		39
No Trauma: Spontaneous rupture congenital hydronephrosis		1
Perforation of pelvis by stone		1
No cause		2
Total		4

Of the 4 cases in which there was no history of trauma, 1 followed spontaneous rupture of the pelvis in a child of 15 months with a congenital hydronephrosis (Poulter and Garvey, 1953). Spontaneous rupture of the kidney is a rare event and invariably associated with chronic renal disease (Martineau and Turkel, 1948). Block (1932) reported a case which followed perforation of the renal pelvis by a stone. The third case (Hyman, 1953) had no past history of injury at all, and in the fourth (Nove-Josserand, 1900) the type of injury if present was not indicated.

It is of interest that the appearance of the pseudocyst may follow many years after the initiating injury (Table II). Four years elapsed after injury in the case reported above, and Johnson and Smith (1941) described a case with calcification in the wall of the pseudocyst, in which the renal injury had occurred 37 years before. Conversely, and more commonly, progressive hydronephrotic atrophy of the kidney may follow within a few weeks or months. In this series 28/39 (72 per cent) presented within 2 months of injury.

TABLE II

Latent Period between Injury and Diagnosis

0 to 3 weeks	16
3 weeks to 2 months	12
2 months to 1 year	7
More than a year	4
Total	39

The rarity of pseudocysts after renal operations may be explained on the basis of the factors necessary for the pathogenesis as stated above. Firstly, the local accumulation of any urine that does leak is avoided by adequately placed drains. Secondly, an attempt is usually made to exclude ureteric obstruction at operation by passing a bougie down into the bladder. Obstruction in the early post-operative phase can be avoided in suitable cases by a ureteric tube splint.

Hypertension.—Hypertension is an uncommon complication of pseudocyst. Schroeder and Correa (1966) reported the case of a 17-year-old boy with a left pararenal pseudocyst and a blood pressure of 190/120, occurring 3 months after a football injury to the left flank. His blood pressure was known to have been normal 1 month prior to injury. A renal arteriogram showed displacement and distortion of the left renal artery by the pseudocyst. The peripheral vein renin level was high and the level in the left renal vein blood was shown to be higher than in the right. The hypertension was cured by nephrectomy.

Diagnosis.—Early diagnosis of this rare condition is essential if irreparable damage to the kidney is to be avoided. This is not always easy as the patient is often symptom free in the early stages and there may be no detectable abnormalities in the urine. The history of trauma, with the subsequent development of pain and a renal swelling, is clearly very important.

TABLE III

Radiological Findings

Not done	25
Distortion of calyces, pelvis	14
Non-function	4
Total	43

Plain X-rays usually show a mass in the renal area but as indicated calcification is rare. Intravenous pyelograms (Table III) may show a non-functioning kidney, or a variable degree of hydronephrosis or displacement of the pelvis or ureter. The findings can be clarified by retrograde ureterograms. The 18 cases where radiographs were not obtained were mainly reported in the nineteenth century and first 30 years of this century before radiology was readily available.

Communication of the pseudocyst with the pelvis or ureter was demonstrated in 34/37 cases in which this point was noted (92 per cent). The point of communication was visualised radiologically in 9/26 cases (34 per cent).

Differential Diagnosis.—Differential diagnosis of pararenal pseudocyst from other cystic lesions around the renal sinus, causing pelvi-calyceal distortion, may be difficult.

Encysted perinephric hæmatoma, also arising as a complication of renal trauma, may be impossible to differentiate pre-operatively. There is no communication with the renal pelvis and histologically the wall shows deposits of hæmosiderin.

Parapelvic cysts produce a more smooth deformity of the pelvis. They do not communicate with the collecting system (Abeshouse and Abeshouse, 1961). On intravenous pyelography they may be surrounded by a radiolucent zone due to compression of the sinus and perinephric fat (Shapiro, 1963). At operation they are thin walled, bluish and lack the marked surrounding fibrosis that characterises the pseudocyst. Histologically, they have an endothelial lining consistent with their probable origin from lymphatics.

Pelvic diverticulum is a rare congenital lesion, smooth walled and communicating with the renal pelvis. It rarely gives rise to symptoms.

TABLE IV

Communication with Renal Pelvis

Communication:	demonstrated	34
	not shown	3
	not stated	6
Total		43

TABLE V

Management and Results

Deaths before operation		5		
Primary nephrectomy		16		
Drainage:	cured	2		
	uncertain	1		
	failed	10	Secondary nephrectomy	4
			Autonephrectomy	2
			Uncured	4
Ureterolysis		9 cured		

TABLE VI

Age Incidence

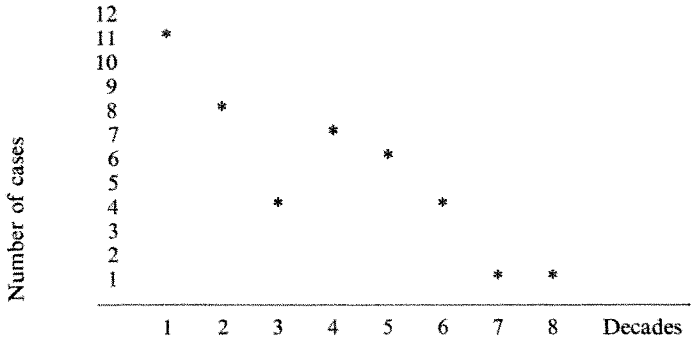


TABLE VII—Summary of 43 cases

Author	Age Sex	Trauma		Time to Diagnosis	X-rays*	Communication Demonstrated	Management	Result	Further Operation
		Blunt	Operative						
Hawkins, 1834	M 6	+		10 days	–	+		Died	
Vincent, 1844	F ?	+		? days	–	+		Died	
Holmes, 1861	F 37	+		2 yrs	–	+		Died	
Barth, 1876	F 70	+		9 days	–	+		Died	
Cabot, 1883	M 10	+		? weeks	–	?	Repeated puncture	Uncured	
Barker, 1885	M 3½	+		2 mths	–	+		Died	
Morris, 1894	M 30	+		6 days	–	?	Drained	Uncured	
Mudd, 1899	? 5	+		16 days	–	+	Drained	Uncured	
Chaput, 1899	M 16	+		10 days	–	+	Drained	Uncured	Nephrectomy
Le Dentu, 1900	M 23	+		3 days	–	+	Drained	Uncured	
Le Dentu, 1900	F 30	+		16 days	–	?	Drained	Uncured	Nephrectomy
Nove-Josserand, 1900	F 8½	?		2 days	–	?	Drained	?	
Picard, 1921	? 6	+		32 days	–	+	Nephrectomy		
Kaiser, 1921	M 24	+		12 days	–	+	Nephrectomy		
Bianchetti, 1927	F 16	+		immed.	–	+	Repair	Cured	
Nisio, 1928	F 12	+		5 days	D	+	Drained	Uncured	Nephrectomy
Danum, 1932	M 34	+		10 days	D	+	Nephrectomy		
Block, 1932	M 52	Stone in pelvis		immed.	–	+	Drainage + ureteric catheter	Cured	
Bennoit *et al.*, 1913	F 44	+		2 mths	–	+	Nephrectomy		
Stirling, 1934	M 28	+		26 days	D	+	Drained	Cured	
Crabtree, 1935	M 5	+		14 days	D	+	Drained + pedicle ligated		Autonephrectomy
Crabtree, 1935	F 13	+		4 mths	D	+	Drained		Autonephrectomy
Crabtree, 1935	F 8	+		14 days	D	+	Drained + pedicle clamped		Autonephrectomy
Johnson, C. M., 1941	F 41	+		37 yrs	NF	+	Nephrectomy		
Seright, 1950	M 3	+		9 wks	D	+	Ureterolysis + reimplant ureter	Cured	
Hyman, J., 1953	F 58	–	...	...	D	–	Ureterolysis	Cured	
Poulter *et al.*, 1953	M 15 mths	–	Hydronephr.	...	NF	+	Nephrectomy		
Pyrah *et al.*, 1953	M 12	+		10 wks	NF	+	Nephrectomy		
Pyrah *et al.*, 1953	F 39		P'lithotomy	4 days	NF	+	Nephrectomy		
Crosby, 1959	F 10	+		2 days	D	+	Nephrectomy		
Sturdy *et al.*, 1960	M 2	+ +		11 days	D	+	Ureterolysis + reimplant ureter	Cured	
Sauls *et al.*, 1962	M 37			5 wks	D	+	Nephrectomy		
Sauls *et al.*, 1962	M 20		Pyeloplasty	6 mths	NF	+	Nephrectomy		
Sauls *et al.*, 1962	M 57		P'lithotomy	2 yrs	NF	–	Ureterolysis	Cured	
Sauls *et al.*, 1962	M 44		U'lithotomy	2 mths	D	+	Ureterolysis	Cured	
Weintraub *et al.*, 1964	F 41		Gynæ. op.	4 mths	NF	+	Nephrectomy		
Weintraub *et al.*, 1964	F 40		Gynæ. op.	4 mths	D	?	Nephrectomy		
Weintraub *et al.*, 1964	M 49		U'lithotomy	2 mths	D	+	Boari flap	Cured	
Schroeder *et al.*, 1966	M 17	+		3 mths	D	–	Nephrectomy		
Hudson *et al.*, 1967	F 53		P'lithotomy	6 wks	D	+	Drained + ureteric catheter	Cured	
Hudson *et al.*, 1967	F 30		P'lithotomy	2 mths	D	?	Nephrectomy		
Hurwitz *et al.*, 1967	F 9	+		2 mths	NF	+	Nephrectomy		
Arnold	F 69	+		4 yrs	D	+	Ureterolysis		

D = Deformity *NF = Non-function

Management.—Since most reported cases follow blunt injury to the kidney, careful follow-up of all such patients can be expected to lead to an earlier diagnosis. Serial I.V.P.s are particularly important in those in whom a tear in the pelvis with extravasation of contrast material has been demonstrated on the initial post-injury films. An I.V.P. should be performed 2 to 3 months after any operation on the renal pelvis and ureter, to assess the effectiveness of the operation, and the restoration of satisfactory anatomy and function.

For the established condition, nephrectomy was performed as the primary treatment in 16 cases, and as a secondary operation in 4 others in which conservative surgery was unsuccessful (Table V). Conservative operations consisted of excision of the pseudocyst with ureterolysis. Simple drainage in the early cases was highly unsatisfactory. In one of the two cases where drainage was curative a ureteric catheter was used in conjunction (Hudson *et al.*, 1967).

SUMMARY

A case of pararenal pseudocyst has been present. The pathogenesis, diagnosis and treatment have been discussed in the light of 43 cases reviewed from the literature.

I wish to thank Mr P. F. Philip, MS., FRCS., under whose care this patient was admitted to the West London Hospital (Charing Cross Group) and who performed the operation, for permission to present this case.

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PRIMARY TUMOURS OF THE RETRO-VESICAL REGION WITH SPECIAL REFERENCE TO MESENCHYMAL TUMOURS OF THE SEMINAL VESICLES

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Primary tumours of the seminal vesicles are extremely rare and mesenchymal tumours are less frequently encountered than those of epithelial origin. Recently we have had the opportunity of studying 2 cases of primary mesenchymal tumours arising in, or in the region of, the seminal vesicles.

CASE HISTORIES

Case 1.—Mr S. J. J., aged 57 years, was admitted on 7th December 1969, having been unable to pass urine for 6 hours. For 2 weeks he had been troubled with pain in the lower abdomen, burning micturition and frequency. He had been passing urine 6 times during the night. There had been no hæmaturia. His weight was steady and appetite good. There was a visible swelling in the lower abdomen which was thought to be a distended bladder, but on catheterisation only 350 ml. of clear urine was obtained and an abdominal mass persisted. On rectal examination the prostate felt enlarged and benign, but the examining finger could not reach its upper border.

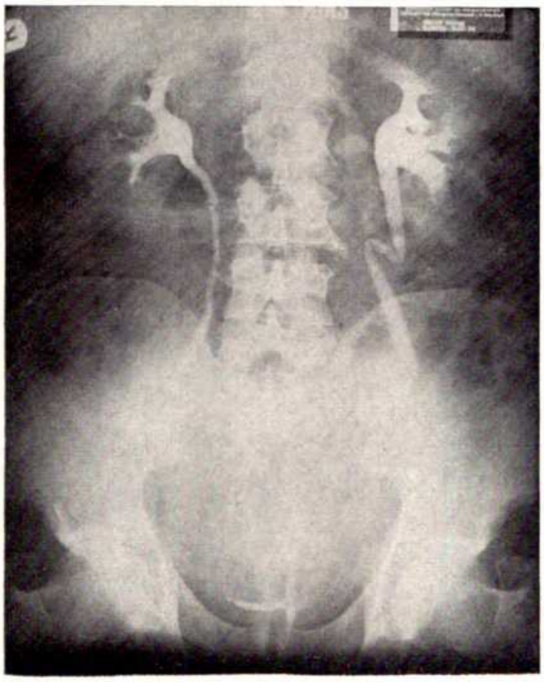

Fig. 1

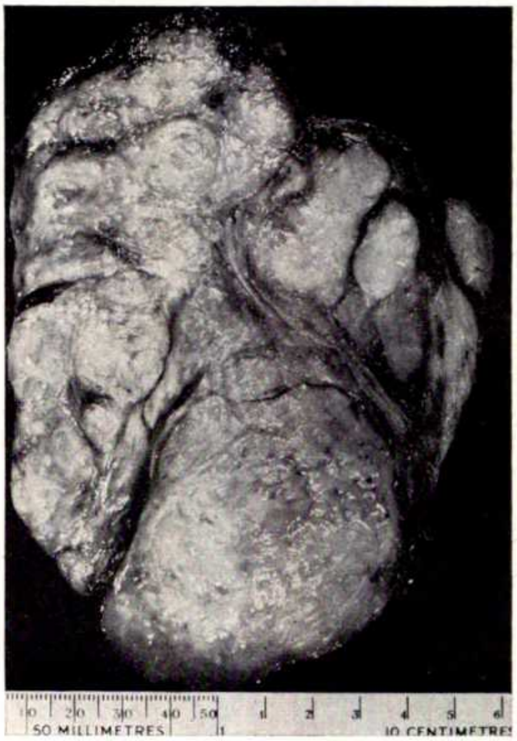

Fig. 2

Fig. 1.—Case 1. I.V.P. showing displacement of and obstruction to ureters from soft tissue swelling arising from the pelvis.

Fig. 2.—Case 1. Gross appearances of specimen.

Serum urea—23 mg. per cent. M.S.U.—normal. I.V.P. (Fig. 1)—A soft tissue shadow was seen in the pelvis with some lateral displacement of, and obstruction to, the lower ends of the ureters. Cystoscopy could not be performed as the beak of the instrument could not be introduced into the bladder. Radiograph of chest normal.

Operation.—10th December 1969 (Mr J. R. Geddes). The lower abdomen was explored through a paramedian incision. Behind the bladder a large mass was present arising from the region of the seminal vesicles. The tumour was dissected free and removed with some difficulty. The prostate was not involved and appeared of normal size.

The patient made a satisfactory recovery from the operation and at a follow-up examination on 29th May 1970 he was quite well, passing urine normally and showed no evidence of tumour recurrence.

Pathological examination (Fig. 2).—The tumour measured 14 × 6 cm., and had a lobulated structure with a pale grey surface and firm texture. It was enclosed in a fibrous capsule and was adherent to the seminal vesicles. Microscopically the tumour was a fibrosarcoma showing moderate cellular pleomorphism but relatively low mitotic activity.

Case 2.—Mr E. H. F., aged 42 years, was seen in April 1969 complaining of diurnal frequency only. He had previously been treated for osteomyelitis of the left iliac bone and examination revealed scars in the region of the left groin. On rectal examination the prostate felt normal, but a tense, rounded swelling was palpable just above the gland.

Serum urea—34 mg. per cent. Hb. estimation—14·9 g. per cent. M.S.U.—normal. I.V.P.—normal. Cystoscopy revealed a moderate degree of trabeculation, but was otherwise normal.

Operation (R. E. S.).—19th November 1969. The lower abdomen was explored through a lower paramedian incision. A firm, rounded mass 5 cm. in diameter behind the bladder, attached to the right seminal vesicle and crossed by a thickened vas, was removed. Recovery was uneventful.

Pathological examination.—The specimen was a cystic nodule 5 cm. in diameter attached to the seminal vesicle. It contained mucinous material. Microscopically the appearances were unusual. The tumour was thought to be a leiomyoma of vascular origin which had undergone myxomatous change. There was no evidence of frank malignancy, but follow-up was advised as there was some suggestion of sarcomatous potential.

DISCUSSION

In both these cases the tumour was closely related to a seminal vesicle and a portion of this structure was removed with the specimen. As in other reported cases it is impossible to be certain that the tumours originated in that organ and conceivably they may have arisen in the connective tissue, blood vessels or neural structures of the retro-vesical space.

Sarcoma of the Seminal Vesicle.—A review of malignant connective tissue tumours of the urogenital system in adults by Tripathi and Dick in 1969 included only 4 cases of sarcoma of the seminal vesicle.

Zahn in 1885 reported the first case of primary sarcoma. The patient, a 76-year-old man, had died from widespread metastases and at autopsy a primary tumour involving both vesicles and the size of a cherry was found.

The second case was reported by Junghanns in 1930. The patient was a 48-year-old man whose 2 months' illness ended fatally after a subtemporal decompression for cerebral symptoms. Autopsy disclosed a firm tumour arising from the left seminal vesicle with multiple hæmorrhagic metastases in both occipital lobes, in the basal ganglia and the cerebellum. The histological diagnosis was " large cell alveolar sarcoma of the left seminal vesicle ", but Willis (1967) questions the authenticity of this case and thinks it was an anaplastic carcinoma.

Lazarus reported the third case in 1946. A man of 47 years presented with a 6 months' history of pain in the rectum and buttock and loss of appetite. There were no symptoms referable to the genito-urinary tract. Rectal examination revealed a small elastic prostate gland which appeared to be compressed from above downwards by a large mass which was ovoid in shape, and extended across the recto-vesical pouch above the base of the prostate. The tumour, which was covered by normal rectal mucosa, reached upwards into the pelvis as far as the examining finger could reach. At operation a large tumour with a thick fibrous capsule partically covered with peritoneum was present in the region of the seminal vesicles. It was firmly adherent to the neighbouring structures which precluded total extirpation. The soft brain-like tumour was spooned, curetted and aspirated out and the cavity washed with 50 per cent ethyl alcohol and packed with sulphanilimide crystals. Histologically the tumour was a pleomorphic cell sarcoma containing numerous mitoses. Radiotherapy in a dose of 6,000 r. was administered. At the completion of the treatment a recurrent tumour in the region of the left seminal vesicle was removed through the perineal route and radon seeds implanted at the site. Two years later the patient was well and free from recurrence.

Tripathi and Dick (1969) reported a case of leiomyosarcoma arising from the region of the right seminal vesicle. They do not elaborate on the clinical history of the case but state that the case resembled the one described by Lazarus.

Gutierrez (1942) classifies sarcomata situated behind the bladder as—

(1) tumours which take origin in the retro-vesical connective tissue structures and which definitely involve the seminal vesicles;
(2) sarcomata which arise in the prostate gland and invade the neighbouring structures.

Young (1926) groups them collectively as tumours of the retro-vesical space. Lazarus subscribes to Young's view and believes it impossible clinically, histologically or at autopsy to be absolutely certain of the exact point of origin of these tumours.

Benign Connective Tissue Tumours of the Seminal Vesicle.—In 1910 Emmerich reported the first case of cystomyoma of the seminal vesicle. Since then isolated cases of benign tumours such as myomas, cystadenomas, cystomyomas and fibromyomas have been described. The Survey of Tripathi and Dick of the records of the Lahey Clinic Foundation, the New England Deaconess and New England Baptist Hospitals over a 45-year period (1923-1968) yielded only 1 case of leiomyoma of the seminal vesicle.

A case of leiomyoma of the seminal vesicle was described by Pana in 1930 (cited by Plaut and Standard, 1944). The patient was a 59-year-old man in whom a pear-shaped retroperitoneal mass attached to the left seminal vesicle was found at autopsy. The gross and microscopical picture was that of myoma. Plaut and Standard report a case of cystomyoma of the seminal vesicle. In common with other authors, they regard such tumours as developmental in origin, arising in the remnants of the mid-portion of the Mullerian duct which normally disappears early in the embryonic life, and point out that these tumours, while based on malformation, become manifest late in life. Their assumption, to some extent, explains the lateral displacement of related structures by the tumour. Lawson and MacDougall (1965), describing an example of multilocular cyst of the seminal vesicle, attributed its source to that organ rather than the Mullerian duct and noted medial displacement of the ureter on pyelography.

Symptoms.—Benign tumours are usually symptomless and may be discovered accidentally at autopsy or operation, as in the case described by Plaut and Standard. This was so in case 2 when the presence of a swelling was discovered by the patient's practitioner carrying out rectal examination for unrelated urinary symptoms. The more rapidly growing malignant tumours may cause symptoms by the displacement of the bladder or other structures as in case 1.

Diagnosis.—Pre-operative diagnosis is extremely difficult and rarely made. The possibility of spread from a tumour of the prostate must be excluded, clinically and later, when histological evidence is available. To assist in diagnosis, Winsbury-White and Fergusson (1961) suggest seminal vesiculography by the technique described by Abeshouse, Heller and Salik (1954). On cystoscopy there may be a bulge into and changes in the appearance of the base of the bladder. Hajdu and Faruque (1968) express the hope that, with the help of refined cytological and histochemical techniques, a specific diagnosis of seminal vesicle tumours will be possible at biopsy.

SUMMARY

1. Two cases of mesenchymal tumour of the seminal vesicle are described.

2. It is difficult to distinguish between tumours arising from the seminal vesicles and those arising from other tissue elements of the recto-vesical space.

3. Mesenchymal tumours of the seminal vesicles are rare and, when small and benign, are usually symptomless and discovered accidentally.

We would like to thank Mr J. R. Geddes, under whose care case 1 was admitted, for permission to include details; Dr W. C. MacCullagh Wilson and Dr J. W. Black for pathological reports; and Mrs J. Jenson for secretarial help.

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PROSTATECTOMY IN HÆMOPHILIA AND CHRISTMAS DISEASE

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Better treatment has resulted in an improved life expectancy for patients with congenital coagulation disorders, and since prostatic obstruction is associated with advancing age it is probable that prostatectomy will be performed increasingly in patients with hæmophilia and Christmas disease.

Prostatectomy is an operation which is regarded as particularly prone to bleeding complications even in non-hæmophiliacs. These complications are generally a consequence of the nature of the operation site, but bleeding may also occur as a result of acquired abnormalities of the fibrinolytic system. The operation is therefore especially hazardous in patients with congenital disorders of blood coagulation such as hæmophilia (factor VIII deficiency) and Christmas disease (factor IX deficiency) in whom even minor surgical procedures without adequate coagulation control may provoke catastrophic hæmorrhage and delayed healing.

Therapeutic requirements for successful surgery in patients with coagulation disorders have been defined by Biggs (1966*a*). The nature of the disorder and the severity of the deficiency must be established precisely and the absence of any antibody to the deficient factor must be confirmed since the presence of such an antibody is generally a contra-indication to surgery. Sufficient supplies of the appropriate therapeutic material should be available for maintenance of hæmostasis both during and after the operation. Adequate laboratory facilities are necessary to ensure that the factor assays used for control of treatment are accurately carried out so that it may be known that the required levels of factor VIII or IX are being achieved. A great variety of operations have now been performed in patients with severe bleeding disorders (Tarnay, 1968) and, in general, if the principles outlined above are adhered to the results have been successful. Hæmophiliacs described in the literature who have had prostatectomy, however, have usually suffered severe bleeding complications at or after operation. This paper presents case reports of 5 patients with hæmophilia or Christmas disease who underwent prostatectomy for benign hypertrophy of the prostate gland and were treated in Oxford. Past literature on the subject is reviewed.

Therapeutic Materials.—*Cryoprecipitate* was produced from fresh frozen plasma by the method of Pool and Shannon (1965).

Human factor VIII concentrate (*human antihæmophilic globulin, human AHG*) was made either by the ether fractionation method of Kekwick and Wolf (1957) or by a modified Blombäck (1958) procedure.

Porcine and bovine factor VIII concentrates (*porcine and bovine AHG*) were purchased from Maws Pharmacy Supplies, Barnet, Herts, where they were made by modifications of the methods of Bidwell (1955*a*, *b*).

Human factor IX concentrate was made in Oxford by the method described by Bidwell and Dike (1966) and in France by the method of Soulier *et al.* (1969).

The choice of material depends upon its availability and the requirements of the individual patient. It is the present practice in Oxford to use cryoprecipitate for replacement therapy during and after surgery and human AHG for any supplementary doses that may be required. Animal AHG is usually only indicated when therapeutic material of human origin is in short supply. Factor VIII of animal origin may induce severe reactions in the patient and thrombocytopenia is a common complication of therapy. Both bovine and porcine AHG usually produce diminishing responses to doses after about a week of treatment. The cause of this resistance to therapy is not known and antibodies to factor VIII have not been demonstrated. All factor IX concentrates are of human origin.

Diagnostic and Therapeutic Methods.—Any patient suspected of having a hæmorrhagic disorder should be fully investigated before surgery. Investigations should include a full personal and family history, examination and laboratory tests, as described by Biggs (1966*b*).

Biggs (1966*a*) has recommended that levels of factor VIII should be constantly maintained above 20-25 per cent of average normal during surgery and the initial stages of wound healing. If doses are given once a day, a post-infusion level of about 100 per cent must be obtained since the half-life of factor VIII is approximately 12 hours. The post-transfusion levels required for factor IX replacement are probably somewhat less since the half-life of factor IX is between 18 and 24 hours. Such levels can only be obtained by the use of concentrated materials and for the first few days after major surgery it is advisable to give 2 or 3 doses every day, both to maintain adequate levels and to conserve material, since the more frequently doses are given the less total material has to be used to maintain a particular minimum level. The amount of therapeutic material needed to attain the required level of factor VIII or IX was calculated as described by Biggs and Matthews (1966).

CASE REPORTS (Table I)

Case 1.—E. H., aged 60, had severe Christmas disease (0 per cent factor IX) with a history of numerous hæmarthroses and severe bleeding on 2 occasions after dental extractions. He had suffered many episodes of spontaneous hæmaturia, but in 1964 was admitted complaining of hæmaturia associated with progressive frequency, urgency and dysuria for the previous 3 years. Cystoscopy showed that the left lobe of the prostate was enlarged.

A retropubic prostatectomy was performed after prior infusion of factor IX concentrate. Factor IX replacement therapy was continued for 31 days, concentrate being given daily for the first 12 days and fresh frozen plasma thereafter. Following operation there was considerable hæmaturia with clots and this continued for 26 days, gradually decreasing in amount and finally stopping after a further 4-day course of factor IX concentrate. The patient was discharged well on the 37th post-operative day.

Five months after discharge he complained of increasing dysuria, nocturia, straining and micturition stopping in mid stream. A transvesical resection of the bladder neck was performed with dilatation of a urethral stricture, treatment with factor IX concentrate being given for the first 13 days and with fresh frozen plasma until the 19th post-operative day. There was slight oozing of blood from the abdominal wound on the 7th day and mild hæmaturia from the 16th to the 19th days which stopped after treatment with epsilon-aminocaproic acid (EACA). He was discharged well on the 40th post-operative day.

Case 2.—C. B., aged 58, a severely affected hæmophiliac with 0 per cent factor VIII, was admitted with acute retention of urine and an enlarged prostate was found on examination. Hæmophilia had been diagnosed in infancy. He bruised excessively, had had many hæmarthroses and several episodes of hæmatemesis and had bled for up to 10 days after dental extractions. From the age of 20 he had had numerous episodes of hæmaturia, usually without any precipitating cause.

A transvesical prostatectomy was performed after an infusion of porcine AHG. Two doses of porcine AHG were given on the day of operation and a single dose was given on each of the next 8 days. These doses initially maintained the factor VIII level at over 40 per cent of average normal. Because resistance developed to porcine AHG, a dose of bovine AHG was given on the 9th and 10th post-operative days, but this had to be discontinued because of severe reactions and poor response. Thereafter, for the next 3 days, human AHG was given in the form of concentrate in the morning and fresh frozen plasma in the evening, good responses being measured after the infusions.

The patient was discharged well on the 34th post-operative day.

Case 3.—J. S., aged 64, had mild Christmas disease with a factor IX level of 8 per cent of average normal and little history of excessive bleeding. He was admitted with acute retention of urine and although catheterisation relieved his obstruction it provoked hæmaturia which continued despite daily treatment with fresh frozen plasma for 2 weeks. Cystoscopy showed that the prostate was enlarged.

A transurethral resection was performed under cover of factor IX concentrate, but because of heavy bleeding associated with a prolonged operation to remove large quantities of debris from the bladder, resection was incomplete.

During the first 7 days following the operation there were 2 episodes of urinary obstruction unassociated with hæmaturia or blood clots and the operation was therefore repeated. Following this second operation his recovery was uneventful. Therapy with factor IX concentrate was given for a total of 20 days.

TABLE I

Oxford Cases

Case	1 (1st operation)	1 (2nd operation)	2	3	4	5
Year of operation.	1964	1965	1965	1966	1967	1970
Age at operation (years).	60	60	58	64	67	56
Deficient factor and level.	0% IX	0% IX	0% VIII	8% IX	6% VIII	4% VIII
Type of operation.	Retropubic.	Transvesical resection of the bladder neck and dilation of a urethral stricture.	Transvesical.	Transurethral (twice).	Retropubic.	Retropubic.
Therapeutic materials used.	IX. Concentrate. Fresh frozen plasma.	IX. Concentrate. Fresh frozen plasma.	Porcine AHG. Bovine AHG. Human AHG. Fresh frozen plasma.	IX. Concentrate.	None during operation. Two weeks after operation—porcine AHG, human AHG, cryoprecipitate. Fresh frozen plasma.	Cryoprecipitate. Human AHG.
Average minimum levels for 1st 7 days after operation.	25%	25%	33%	1st operation 24% 2nd operation 22%	6%	41%
Total period VIII or IX therapy (days).	31	20	19	20	36	21
Blood transfused (units of whole blood + packed cells).	7	1	12	7	32	Nil
Total period hæmaturia after operation (days).	26	4	6	1	36	20
Other complications.	Urinary infection. Urethral stricture and obstruction leading to 2nd operation.	Urinary infection. Slight oozing of blood from abdominal wound.	Urinary infection. Mild hæmolysis.	1st operation was incomplete. Obstruction leading to 2nd operation. Urinary infection.	Not diagnosed before operation. Two repeat operations to control heavy bleeding. Clot retention. Delayed wound healing. Urinary infection.	Clot retention.
Time in hospital after operation (days).	37	40	34	22	87	24

Case 4.—M. S., aged 67, was not known to be a hæmophiliac. He presented at another hospital with acute retention of urine and a grossly enlarged prostate was felt on rectal examination. At the age of 7 years a leg abscess was incised and the wound bled for several days. He bled heavily after removal of 4 teeth in adolescence. His brother had had prolonged hæmorrhage after prostatectomy.

A retropubic prostatectomy was performed without factor VIII replacement. Following the operation there was continued heavy bleeding. Laboratory tests showed no evidence of hypofibrinogenæmia. He returned to the theatre 7 hours later and the wound was reopened. The skin was bruised, the wound hæmorrhagic and the floor of the bladder was oozing blood. One bleeding point was ligated and the prostatic cavity was packed. For the next 2 weeks heavily blood-stained urine continued to drain suprapubically and through the urethral catheter. There were 3 episodes of retention which necessitated evacuation of blood clots under general anæsthesia, but on the third occasion it was not possible to evacuate the clots per urethram. The wound was reopened, there was a hæmatoma in the anterior abdominal wall and a large amount of blood clot was found in the retropubic space.

Investigations showed that the patient had a factor VIII level of 6 per cent of average normal and was therefore a moderately affected hæmophiliac. He was transferred to Oxford, where he was given a 14-day course of porcine AHG. Hæmaturia diminished but did not clear completely until he had had a further 11 days' treatment with human AHG. The suprapubic wound healed very slowly at first with much leakage of urine, which increased in volume on each of several episodes of clot retention. Nineteen days after cessation of factor VIII therapy heavy hæmaturia recurred and a further course of human AHG was given for 11 days. Following this there was no further hæmaturia. Subsequent progress was uneventful and he was discharged well 87 days after the original operation.

Case 5.—D. F., aged 56, had had progressive difficulty in micturition for 3 years which culminated in an attack of acute retention 1 month before admission for prostatectomy. At the age of 7, following tonsillectomy, he bled heavily and required blood transfusion. Dental extractions on 3 occasions were complicated by excessive bleeding and once required blood transfusion. Investigation showed a factor VIII level of 4 per cent.

A retropubic prostatectomy was performed after infusion of cryoprecipitate which was given for the next 20 days. Following the operation, hæmaturia, initially marked, gradually decreased but continued until the 20th day despite increased factor VIII dosage with 2 infusions per day from the 15th to the 17th days. There were 2 episodes of clot obstruction, both relieved by catheterisation. Because of the persistent hæmaturia a course of EACA was started on the 20th day and shortly after the first dose the hæmaturia cleared and remained clear on discharge on the 24th post-operative day.

DISCUSSION AND REVIEW OF PAST LITERATURE

Patients described in early reports of prostatectomy who were not treated with concentrated materials suffered severe bleeding complications (Table II). After fulguration of bladder polypi and the median lobe of the prostate, the patient of Mathé and Mitchell (1929) had several severe hæmorrhages which necessitated cystotomy. The abdominal wound was left open so that hæmostatic substances could be applied locally and general measures to control blood coagulation included an induced anaphylactic shock reaction with rabbit serum. The patient spent over 2 months in hospital. The patients reported by Hinman (1933), Young and Sacks (1957), Owen *et al.* (1962) and Kerr (1964) all required multiple blood tranfusions following prostatectomy. Significantly, the patient of Irwin *et al.* (1962), an infant who underwent Bradford-Young bladder neck revision for congenital contracture of the bladder neck and hypertrophy of the trigone, developed minimal bleeding complications. This child was given Cohn's fraction I (Cohn, *et al.* 1946), an early human AHG concentrate, during and for 12 days after the operation.

The 26-year-old Negro hæmophiliac described by Bulloch *et al.* (1957) developed urinary obstruction following prostatic massage and prostatectomy was performed after infusion of fresh frozen and lyophilised plasma, the criterion of adequate coagulation control being a corrected whole blood clotting time. The post-operative course was " stormy " and there were several episodes of shock. The whole blood-clotting time is of little use either in diagnosis or control of therapy during surgery, since it may be corrected with as little as 2 per cent of factor VIII. Patients with mild or moderate hæmophilia or Christmas disease will have more than this level of factor VIII or IX but will almost certainly still bleed heavily after surgery. It is always necessary to employ specific assays for factors VIII or IX when controlling therapy during surgery in patients with hæmophilia and Christmas disease.

TABLE II

Cases Reviewed from Past Literature

Case	Mathé and Mitchell (1929)	Hinman (1933)	Young and Sacks (1957)	Bulloch, Johnson and Davis (1957)	Owen, Thompson and Bowie (1962) (2 cases)	Kerr (1964)	Irwin, Liles and Blanchard (1962)
Year of operation.	1926	1931	1955	1957	1956-1961	1961	1961
Age at operation (years).	57	66	56	26	Not stated	64	6 months.
Type of operation.	Transurethral.	Perineal.	Perineal.	Perineal.	Transurethral.	Transurethral.	Transvesical.
Therapeutic materials.	Blood. Local silver nitrate and anti-pyrine. Anaphylactic shock with rabbit serum. Calcium lactate.	Blood.	Fresh plasma. Fresh blood.	Fresh plasma. Fresh frozen plasma. Lyophilised plasma.	Plasma. Blood.	Fresh frozen plasma. Blood.	Cohn's Fraction I. Lyophilised plasma. Fresh blood.
Complications.	Severe hæmorrhage on several occasions. Cystotomy required.	Extensive bleeding from urethra and wound. Delayed wound healing.	Extensive bleeding leading to rectal obstruction. Perineal fistula Epididymitis. 34 units of blood transfused.	" Stormy " with several episodes of shock. 28 units of blood transfused.	Not stated. " Extensive therapy."	Not stated. 9 litres of blood transfused.	Hæmaturia only.

The majority of patients who have unexpected bleeding complications after surgery due to congenital disorders of coagulation are only mildly or moderately clinically affected and do not always have a past history of bleeding. Owen *et al.* (1962) reviewed 1,416 patients who underwent surgery between 1956 and 1961 and were investigated for blood coagulation function. Of the patients investigated during or after operation for the first time because of unexpected hæmorrhage, and who were found to have definite coagulation defects, only 17 of 34 had a personal or family history of bleeding. Between 1963 and 1969, 19 patients with congenital coagulation disorders were transferred from other hospitals to Oxford because of severe bleeding complications after surgery. Case 4 described in this paper was one of these patients. Four of the 19 had 0 per cent of the deficient factor and were classified as clinically severely affected. The remainder had levels between 2 and 22 per cent of average normal and therefore were only moderately or mildly affected. Eight of the 19 patients were treated during and after operation with some form of therapeutic material, but in insufficient dosage to prevent hæmorrhage. A patient with a low factor VIII or IX level will bleed heavily after surgery and concentrated materials are always necessary to ensure hæmostasis.

The average duration of factor VIII or IX therapy in the Oxford cases was about 3 weeks. Minimum levels of the deficient factor were maintained at over 25 per cent for the 1st week after operation and thereafter the dosage was gradually reduced, unless there was a complication requiring additional treatment. Case 5, who had average factor VIII levels of over 40 per cent average normal during the 1st week, required no blood transfusion at all. It is present practice in Oxford to attempt to achieve higher minimum levels than the 25 per cent recommended by Biggs (1966*a*) and to aim for minimal levels of the order of 35-40 per cent for the 1st week after major surgery such as prostatectomy.

The post-operative course of all the Oxford patients was complicated by hæmaturia and in 2 cases by clot obstruction. Increasing the dosage of factor VIII or IX was not found to be a reliable way of stopping hæmaturia. McNicol *et al.* (1961) showed that treatment with EACA reduced the duration and severity of hæmaturia in patients without coagulation disorders after prostatectomy. The rationale of using EACA to treat post-operative hæmaturia is to inhibit fibrinolysis, so allowing fibrin clots to persist longer on healing wounds. Because of the dangers associated with the use of EACA to treat spontaneous hæmaturia in hæmophiliacs (McNicol *et al.*, 1961; Gobbi, 1967), there has been reluctance in Oxford to treat post-prostatectomy hæmaturia in hæmophiliacs with EACA until there has been a trial of increased dosage of factor VIII or IX replacement without success, even though the 2 situations are not strictly comparable.

No conclusion can be drawn from the patients described here concerning the most suitable type of operation. Provided the coagulation defect can be controlled, the surgeon may choose the operation which would be most suitable in a normal patient.

With meticulous surgical technique and coagulation control it is feasible to perform prostatectomy in patients with hæmophilia and Christmas disease, although bleeding complications are still more likely than in normal patients.

SUMMARY

The case histories of 5 patients with hæmophilia or Christmas disease who underwent prostatectomy and were treated in Oxford are described and a further 7 cases from the literature are reviewed. After accurate diagnosis of the type and severity of the coagulation disorder the operations in the Oxford cases were performed with prior replacement of the appropriate factor in concentrated form. Therapy was controlled by specific assays for factor VIII or IX and continued for about 2 to 3 weeks to ensure hæmostasis, minimum levels of factor VIII or IX in the first post-operative week not being allowed to fall below 25 per cent. Insufficient replacement therapy in cases reported in the literature resulted in severe bleeding complications. Prolonged hæmaturia following the operation was treated initially with increased dosage of the appropriate factor, but if this was unsuccessful a course of epsilon-aminocaproic acid (EACA) was given.

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ENDOMETRIOSIS OF THE URETER

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OBSTRUCTIVE uropathy secondary to endometriosis of the ureter has been reported sporadically since Cullen (1917) first described an example of bilateral involvement of the ureter. Abeshouse and Abeshouse (1960) cited 15 cases of ureteric endometriosis, and 9 years later, Bates and Beecham were able to collect a total of 64 cases from the literature. Brooks, Fraser and Lucas (1969) have described two further examples. The rise in the number of reported cases during the last decade may represent an increased awareness of this unusual manifestation of endometriosis, and also may partly reflect the increasing incidence of endometriosis, which has been aptly described as a twentieth-century disease (Green, 1966).

Five cases seen between 1954 and 1970 are described, and the clinical features and surgical management discussed in the light of previously reported cases. Two of the present series are of particular interest for the occurrence of bilateral ureteric endometriosis in one and carcinomatous change in the endometrioma involving the ureter in the other.

CASE REPORTS

Case 1.—Mrs E. D., a 59-year-old multipara, presented with a 6 months' history of increasing lower abdominal distension and discomfort. There were no urinary or bowel symptoms, and her periods had ceased. On examination the lower abdomen was distended by a firm, smooth swelling arising out of the right side of the pelvis. A diagnosis of ovarian cyst was made.

Management.—At operation there was a large right-sided ovarian cyst which was closely adherent to both Fallopian tubes. The left ovary was also enlarged and cystic. The right ureter adjacent to the ovarian swelling was thickened, dilated and obstructed in mid-pelvis. There was a reduction in the renal cortical tissue on this side. The left ureter was normal and there was no other abnormality in the pelvis. Bilateral oophorectomy was performed with some difficulty because of the mass of fibrosis between the cyst walls and the side walls of the pelvis. The right ureter was reimplanted into the bladder.

Microscopical Examination.—In the right ovary there was a dermoid cyst with extensive foci of endometriosis in its wall. The left ovary contained typical endometriosis.

Progress.—Three months after operation intravenous pyelography showed prompt excretion and a normal ureter on the right side, although the pelvis and calyces were distorted and dilated probably as the result of a long-standing obstruction. The left side was normal. The patient died 10 years later from carcinoma of the breast; the blood urea at this time was normal and the patient had remained well and asymptomatic in the intervening years.

Case 2.—Mrs I. B., a 41-year-old multipara, complained of rectal pain of 4 months' duration. This was particularly severe during menstruation and was associated with an ache in the right iliac fossa and the groin. The patient had also noticed the recent onset of urinary frequency and urgency, unrelated to the menses. On examination the uterus was retroverted and there were tender nodules in the recto-vaginal septum. A hard mass was palpable through the anterior rectal wall. A diagnosis of endometriosis was made.

Management.—Cystoscopy failed to reveal any abnormality and urine culture was sterile. At operation there was extensive endometriosis involving the recto-vaginal septum. The uterus, Fallopian tubes and ovaries were normal. The left ureter was normal and the right was dilated and obstructed by a dense endometriotic mass at the vaginal angle. Total hysterectomy and bilateral salpingo-oophorectomy were carried out and the right ureter was reimplanted into the bladder.

Microscopical Examination.—In the adventitia of the otherwise normal right ureter there were islands of endometrial tissue (Fig. 1). There was no evidence of endometriosis in either ovary.

Progress.—The patient was symptom free 6 months later; however, intravenous pyelography failed to show any excretion from the right kidney. The left side was normal.

Case 3.—Mrs B. T., a 32-year-old nullipara, was referred for investigation of intermittent episodes of hypogastric pain of 6 weeks' duration. These were unrelated to her menstrual cycle, which was normal. There were no urinary symptoms. On examination the uterus was irregularly enlarged and fixed in the retroverted position. A diagnosis of fibromyomata complicated by endometriosis was made.

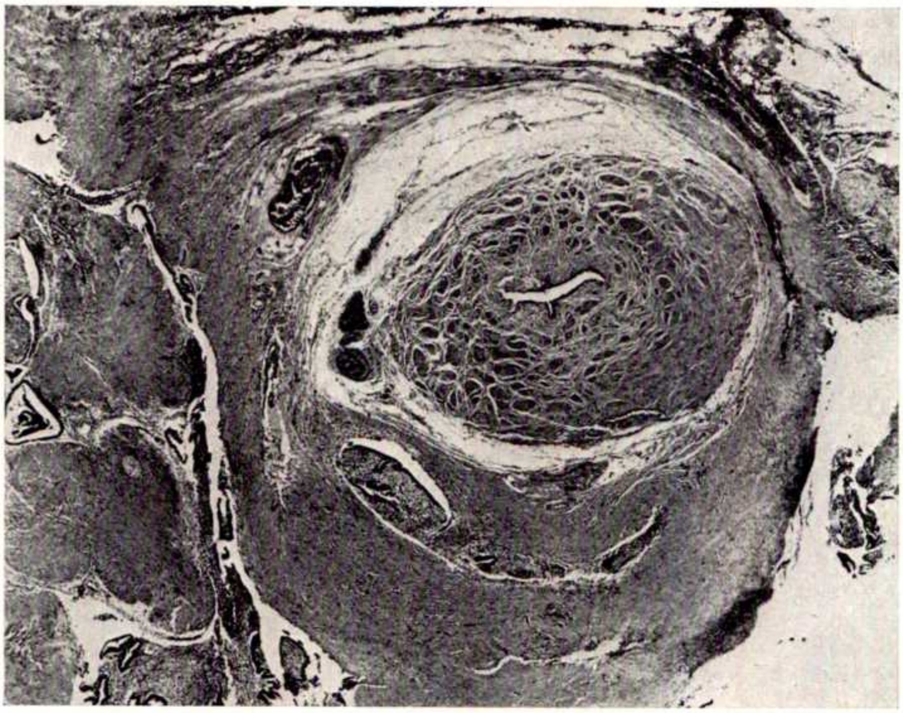


FIG. 1

Case 2. Extrinsic endometriosis. Ureter surrounded by islands of endometrial tissue. H. & E. ×16.

Management.—Total hysterectomy and left partial oophorectomy were performed for fibromyomata and a chocolate cyst of the left ovary. During the mobilisation of the uterus a cystic tumour about 2·5 cm. was seen in the right side in the pouch of Douglas at some distance from the normal right ovary and rectum. Further dissection revealed the right ureter which was obstructed and running through the mass, which had a dense fibrous wall and contained white pultaceous matter. The tumour was excised as completely as possible.

Pathological Examination.—The uterus, apart from fibroids, contained a small endometrial polyp. Microscopical examination showed this to be a simple endometrial polyp without evidence of malignancy. There were several islets of endometriosis on the serosal surface of the uterus and the left ovary also contained foci of endometriosis. Several sections from the cystic mass were assessed. In some areas there was endometrial tissue and in addition there was a poorly differentiated adenocarcinoma lying in connective tissue and muscle.

Further Management.—Radiograph of the chest and barium studies were normal. Laparotomy failed to reveal a primary abdominal site of the tumour. The lymphatic glands on the pelvic wall were dissected and the right ureter was freed with considerable difficulty from the field from which the endometriosis and carcinoma had arisen. Post-operatively the patient was given a course of deep X-ray therapy to the pelvis.

Subsequent histology of the excised tissues failed to reveal any residual growth.

Progress.—Intravenous pyelogram 1 month after surgery was normal. The patient is alive and well without recurrence 17 years later. This case has been presented in greater detail by Ferreira and Clayton (1958).

Case 4.—Mrs B. G., a 31-year-old multipara, first presented in April 1963 with intermittent low left-sided abdominal pain of 1 year's duration. The patient also complained of left-sided dyspareunia and a brown vaginal discharge of recent onset. Her periods were normal and there were no urinary symptoms. Physical examination failed to reveal any abnormality. The blood pressure was 155/100 mm. Hg. On vaginal examination there was a hard mass palpable in the posterior fornix and recto-vaginal pouch.

Management.—Examination under anæsthesia revealed a blue cystic mass extending to the left in the posterior fornix. At laparotomy there was a mass of endometriosis in the recto-vaginal septum, involving the posterior aspect of the uterus and adjacent vagina, the anterior aspect of the rectum and enveloping the left ureter. The ovaries, Fallopian tubes and uterus appeared to be normal. Hysterectomy, including a cuff of the posterior vaginal wall,

FIG. 2

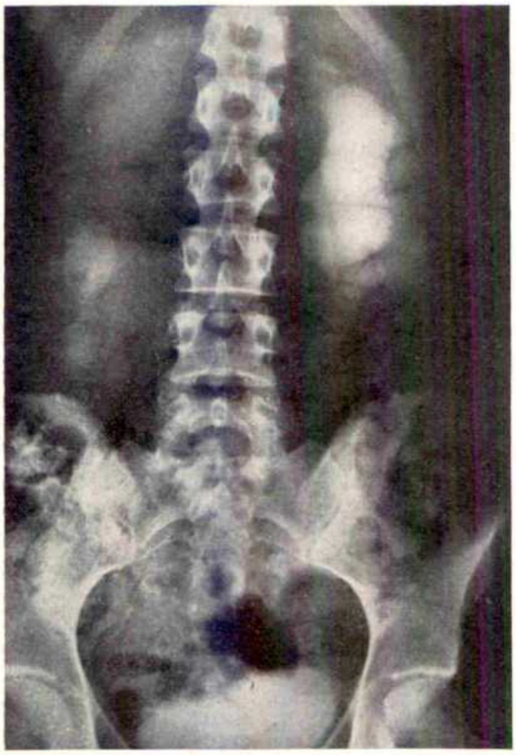
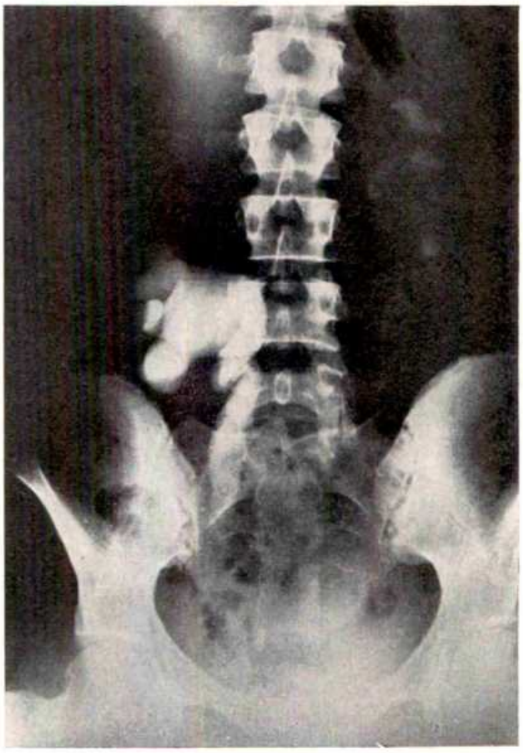


FIG. 3



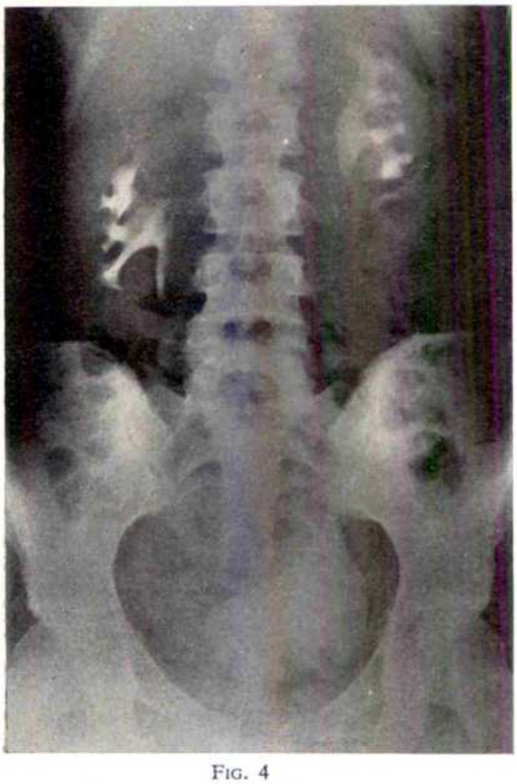


FIG. 4

Fig. 2.—Case 4. High-dose I.V.P. showing bilateral upper tract obstruction. The right ureter is seen to be obstructed in mid-pelvis.

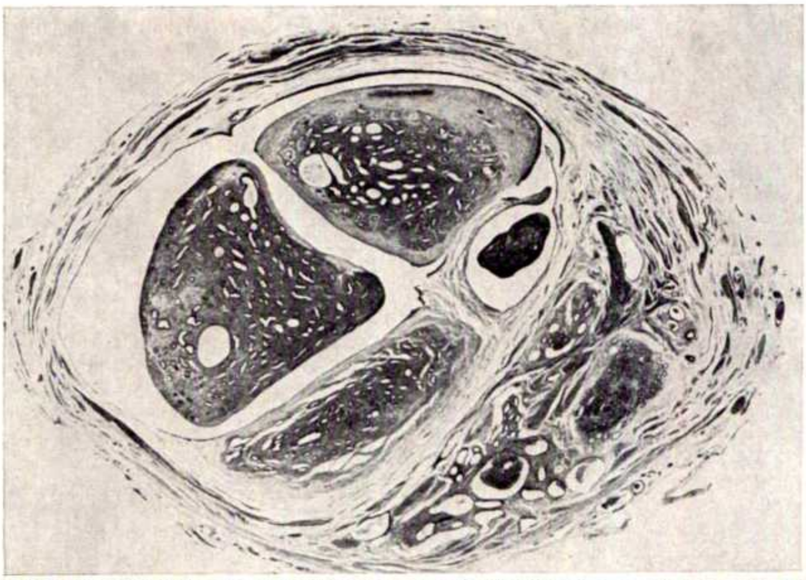
Fig. 3.—Case 4. I.V.P. showing persistent obstruction on right despite ureterolysis and bilateral oophorectomy.

Fig. 4.—Case 4. I.V.P. 2 months after right ureteric reimplantation and 4 months after left ureteric reimplantation.

was performed and the left ureter was dissected free from the endometriotic tissue, which was excised. Postoperatively the patient made an uneventful recovery and was treated with a course of Norethisterone for 3 months.

Histological examination of the excised tissues confirmed the presence of endometriosis involving the fibro-fatty tissue of the recto-vaginal pouch, the posterior wall of the vagina and the cervix.

FIG. 5



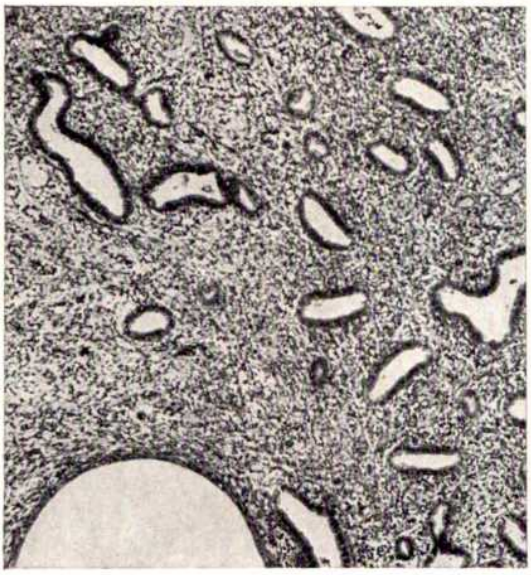


FIG. 6

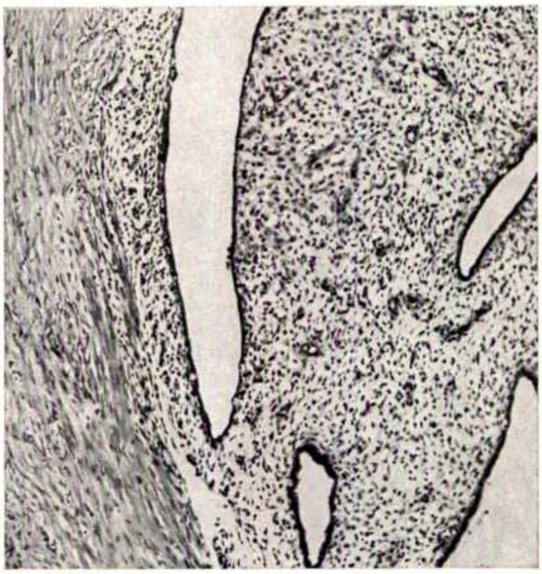


FIG. 7

Fig. 5.—Case 4. Intrinsic endometriosis. Distortion of left ureteric lumen by endometrial tissue infiltrating the wall. H. & E. × 9.

Fig. 6.—Case 4. Left ureter. Endometrial tissue showing inactive glands and stroma. H. & E. × 75.

Fig. 7.—Case 4. Right ureter. Endometrial tissue with cystic glands and pseudo-decidual change of stroma. H. & E. × 75.

The patient was next seen in October 1970 when she was referred with a history of increasing lassitude of 1 year's duration, and the onset of dyspnœa, vomiting, headache and thirst 2 weeks before admission to hospital.

The patient also complained of intermittent episodes of hæmaturia occurring about once a month and associated with the passage of small elongated clots, lower abdominal colic and backache. On examination both kidneys were easily palpable, and the blood pressure was 220/135 mm. Hg.

Investigations.—Hæmoglobin, E.S.R., and chest radiography were normal. The blood urea was elevated at 100 mg./100 ml., while the creatinine clearance was 14 ml./min. E.C.G. showed evidence of left ventricular hypertrophy. There was microscopical hæmaturia; urine culture was sterile. A high-dose intravenous pyelogram (Fig. 2) showed delayed excretion on the left sicde and bilateral hydronephrosis from obstruction of the ureters in the pelvis just above the level of the ischial spines. A radioactive renogram, using I^{125} labelled Hippuran, confirmed the presence of obstruction on both sides with a vascular peak on the right 80 per cent higher than on the left. A diagnosis of bilateral ureteric obstruction resulting from endometriosis was made.

Management.—Cystoscopy was normal. Bimanual examination under anæsthesia revealed the presence of slight thickening on both pelvic walls. At laparotomy both ureters were obstructed by localised plaques of endometriosis adjacent to each ovary. Bilateral oophorectomy was performed. The left ureter was seen to end in a very narrow segment which was excised; the bladder was mobilised and hitched up to the psoas major muscle (Turner-Warwick and Worth, 1969) and the left ureter reimplanted without tension. The right ureter was dissected free from the encasing endometriosis. The patient made an uneventful recovery and was discharged on Gynovlar 21 (Norethisterone acetate and ethinyl oestradiol) 1 tablet daily.

Progress.—The patient remained well. The blood urea fell to 40 mg./100 ml. and the blood pressure to 170/90 mg. Hg. However, 2 months after operation a further intravenous pyelogram (Fig. 3) and a radioactive renogram showed that the right upper urinary tract remained obstructed and unchanged.

Further Management.—The right ureter was explored and it was evident that there had been no benefit from the previous ureterolysis. The narrow segment was excised and the ureter reimplanted into a Boari flap.

Further Progress.—Two months later, the patient was well with a blood pressure of 170/100 ml. and the creatinine clearance was 57 ml./min. A further intravenous pyelogram (Fig. 4) showed that there had been a striking improvement on both sides.

Microscopical Examination.—In the excised left ureter there was infiltration of its wall by endometrial tissue, producing marked distortion of the ureteric lumen (Fig. 5). The endometrial glands were inactive, 1 or 2 being cystic (Fig. 6). The stromal component was normal. There was no evidence of endometriosis in either ovary. A single focus of endometriosis was present adjacent to the fimbrial end of the right Fallopian tube.

Examination of the right ureter removed later showed that there was endometrial tissue adjacent to, but not invading, the wall of the ureter. Cystic changes in the glands were more obvious than in those of the left ureter, but the overall amount of glandular tissue was similar. The stroma showed foci of pseudo-decidual change (Fig. 7).

Case 5.—Mrs H. G., a 41-year-old nullipara, presented with lower abdominal pain and flatulance of 6 months' duration. She complained also of constipation, which was particularly marked during her menses which had been scanty for the previous 4 years. There were no urinary symptoms. Clinical examination failed to reveal any abnormality although the sigmoid colon was easily palpable. On vaginal examination the uterus was tender and retroverted and there was some thickening in the fornices. A diagnosis of endometriosis was made.

Management.—Sigmoidoscopy was normal to 16 cm. At laparotomy the left ovary contained chocolate cysts and there was a firm plaque of endometriosis in the recto-vaginal septum. In the sigmoid colon there was a mass 5 cm. in diameter with the appearances of a carcinoma. Bilateral oophorectomy, sigmoid colectomy and a defunctioning colostomy were performed. During the sigmoid resection it was noted that the left ureter was grossly dilated and obstructed by the plaque of endometriosis in the recto-vaginal septum.

Pathology.—Histology of the left ovary confirmed the presence of endometriosis, while the lesion in the sigmoid colon also proved to be endometriosis.

Progress.—The defunctioning colostomy was subsequently closed, and 5 months later the patient was well and asymptomatic. Intravenous pyelography at this time showed a normal upper urinary tract on the right but on the left there was a well marked hydronephrosis and hydroureter from obstruction of the ureter in the pelvis (Fig. 8).

Further Management.—In view of the persistent obstruction, the left ureter was reimplanted into the bladder.

DISCUSSION

The incidence of urinary tract involvement among patients with endometriosis has been estimated to be about 1 per cent (Dockerty, 1949). Abeshouse and Abeshouse (1960) observed an incidence of 1·1 per cent of vesical endometriosis, while Ball and Platt (1962) found an incidence of 1·2 per cent of ureteric endometriosis in a series of 720 cases of pelvic endometriosis. Ureteric endometriosis is probably more common than generally appreciated, due to its often asymptomatic and unilateral presentation.

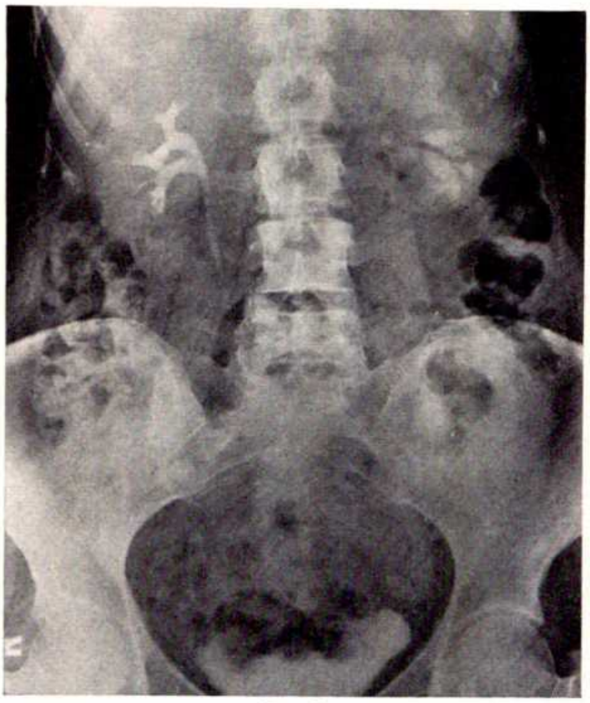


FIG. 8

Case 5. I.V.P. showing persistent left upper tract obstruction 5 months after bilateral oophorectomy. Site of obstruction is clearly shown in mid-pelvis.

Ureteric endometriosis has been classified into extrinsic and intrinsic forms. The extrinsic type is characterised by the presence of endometrial glands and stroma in the adventitia and surrounding connective tissue of the obstructed ureter, while in the rarer intrinsic variety the endometrial glands and stroma are present in the lamina propria or tunica muscularis. The distinction between the 2 forms would seem to be mainly an arbitrary one, the intrinsic probably representing a more advanced invasive state of the extrinsic; in the extrinsic form the depth of invasion has seldom been corroborated by histological evidence (Kerr, 1966). Furthermore, clinically the differentiation is rarely apparent; this is illustrated by case 4 in which the operative appearance of each ureter at the level of obstruction was very similar, although subsequent histological examination showed extrinsic involvement on one side and intrinsic on the other.

Stanley, Utz and Dockerty (1965) postulated that most endometriomas of the bladder and ureter arose by extension from pre-existing pelvic foci, and suggested that ovarian endometriosis was a prerequisite for disease of the ureter. However, in only 2 of the present series was there evidence of co-existent disease in the homolateral ovary. In many instances the obstruction of one or rarely both ureters has been caused by diffuse peritoneal disease. The less common form of obstruction due to an isolated peritoneal implant has been regarded as an example of the dissemination of endometrial tissue through the lymphatics or bloodstream (Bulkley, Carrow and Estensen, 1965). The distribution of other sites of endometriosis in the present series is shown in Table I in conjunction with the findings of Stanley *et al.* (1965). It is interesting to note that the condition has not been recorded in the ureter above the pelvic brim, although it has been described in the kidney on 7 occasions (Hajdu and Koss, 1970).

TABLE I

Other Sites of Endometriosis

	Ovary	Uterine Serosa	Uterus	Peritoneum	Elsewhere
Present series 5 Patients	3	2	2	4	1 colon 1 vagina
Stanely *et al.* (1965) 6 Patients	5	3	0	3	...

TABLE II

Summary of Clinical Features

Case	Age	Side	Symptoms	Pre-op. Diagnosis	Treatment	Result
1	59	Rt.	Lower abdominal distension and pain for 6 months. No urinary symptoms. Post-menopausal.	Ovarian cyst.	Bil. oophorectomy. Reimplantation of right ureter.	Asymptomatic for 10 years. I.V.P.—obstruction relieved.
2	41	Rt.	Rectal, right iliac fossa and groin pain for 4 months. Severe during menses. Frequency and urgency.	Endometriosis.	Total hysterectomy. Bil. salpingo-oopherectomy. Reimplantation of right ureter.	Asymptomatic. I.V.P.—no excretion on right.
3	32	Rt.	Lower abdominal pain for 6 weeks. No urinary symptoms.	Fibroids. Endometriosis.	(1) Total hysterectomy. Left partial oophorectomy. (2) Clearance of pelvic side-wall. Right ureterolysis. D.X.T.	Asymptomatic and well 17 years later. I.V.P.—normal.
4	31	Bil.	Cyclical hæmaturia and clot colic for 1 year. Hypertension. Uræmia. Previous surgery.	Bil. ureteric endometriosis.	(1) Total hysterectomy. (2) Bil. oophorectomy. Psoas " hitch " and reimplantation of left ureter. Gynovlar 21. (3) Reimplantation of right ureter (Boari flap).	Asymptomatic. Reduction in hypertension. I.V.P.—striking improvement. Blood urea normal.
5	41	Lt.	Lower abdominal pain for 6 months. Constipation. Worse during menses. No urinary symptoms.	Endometriosis.	(1) Bil. oophorectomy. Sigmoid colectomy. (2) Reimplantation of left ureter.	Asymptomatic.

Clinical Features.—These have been summarised in Table II. The ages of the patients reported in the literature ranged from 25 to 50 years old and more than 50 per cent were nulliparous. In this series case 1, who was 59 years old and several years post-menopausal, probably illustrates the point that much of the damage caused by endometriosis is due to the subsequent fibrosis. Frank and Geist (1942) observed a significant number of patients with symptomatic endometriosis to be post-menopausal, quoting a figure of 10·6 per cent although this has not been a finding in patients with ureteric endometriosis.

Although the condition was described as long ago as 1917 by Cullen, bilateral involvement of the ureters has been rarely documented (Morse and Perry, 1928; Blaikley, 1962; Simon, Zimet, Schneider and Morgenstern, 1963; Meigs and Sturgis, 1963; Kerr, 1966). In most instances the bilateral disease occurred in cases of wide-spread involvement of the peritoneum or the " frozen " pelvis. Goodall (1944) cited 2 examples in which extensive stromal endometriosis had caused bilateral ureteric obstruction, leading to complete obstruction of the kidneys and death.

Abeshouse and Abeshouse (1960), in stressing the importance of a meticulous surgical technique to prevent implantation of endometrial tissue, reported previous gynæcological or abdominal surgery in 39 of 56 cases with vesical endometriosis. Stanley *et al.* (1965) also noted that 12 of their 19 patients with vesical and ureteric endometriosis had had at least 1 pelvic or abdominal operation. This association was not found in the present series although case 4 had had a previous pelvic operation at which extensive endometriosis was already established.

Ratliff and Crenshaw (1955), in a review of 8 cases, stressed the chronic course of ureteric endometriosis by observing that symptoms had been present for more than 5 years in the majority of their patients. This feature has not been substantiated in the present series (see Table II).

Kerr (1966), in a comprehensive review of 47 cases, found menstrual disorders in 28 per cent, flank pain in 23 per cent, and gross hæmaturia in 13 per cent, and noted abnormal findings on pelvic examination in 50 per cent. Hæmaturia was mainly a feature of cases with intrinsic involvement of the ureter as in case 4. Although endometriosis was diagnosed pre-operatively in 4 out of 5 cases mainly on the basis of abnormal findings on pelvic examination, ureteric endometriosis was suspected only in one due to the lack of specific symptoms referable to the urinary tract. Similarly Stanley *et al.* (1965) observed that a correct pre-operative diagnosis had seldom been made in their patients. Bates and Beecham (1969) recommended that pre-operative pyelograms should be performed in cases of endometriosis severe enough to require surgery, while Kerr (1966) emphasised the value of pyelograms prior to pelvic surgery and exposure of the ureters at the time of operation in establishing the presence of ureteric involvement.

Treatment.—In most cases operative treatment is required for the relief of the ureteric obstruction and to make a definitive diagnosis in a condition in which the reported surgical and autonephrectomy rate approaches 30 per cent. The simulation of malignancy of the ureter has resulted in nephro-ureterectomy, while in other instances the kidney was beyond salvage at the time of presentation. Some authors have favoured castration alone while others have recommended a more aggressive surgical policy. Kerr (1966), in an analysis of the various procedures adopted in the literature, disclosed that ureterolysis had been performed in 32 per cent of which 80 per cent had also been castrated; castration alone was carried out in 21 per cent and resection of the affected ureter with ureteroureterostomy or ureteroneocystostomy in 19 per cent. The author concluded that inadequate subsequent documentation precluded an accurate appraisal of each procedure.

Stanley *et al.* (1965) showed varying degrees of fibrosis of the muscularis or mucosa in 5 out of 6 ureters in their series, and were of the opinion that castration alone was unlikely to be of much benefit. This is supported by the clinical course of case 5 in which the intravenous pyelogram still showed severe obstruction 5 months after surgical castration. O'Conor and Greenhill (1945) have reported that recession of endometrial obstruction did not necessarily follow castration. It would seem that to await regression of the disease and uncertain relief of the obstruction, following castration, has little place in the management of this condition and would invite further unnecessary renal damage.

Brock (1960) stated that the treatment of the intrinsic form of endometriosis was surgical with local excision, while the extrinsic type should be treated by castration, either by surgery, irradiation or hormones, or a combination of irradiation and hormones. Bates and Beecham (1969) have described 2 examples in which irradiation and surgical castration, and also suppressive hormone therapy failed to relieve the obstructed ureter, and suggested that irradiation may worsen the peri-ureteric fibrosis. Case 4 has demonstrated the difficulty in distinguishing between the extrinsic and intrinsic forms of disease and in addition the persistence of ureteric obstruction on one side despite ureterolysis and surgical castration. The latter observation is of particular relevance in bilateral obstruction and clearly there is a strong case for ureteroneocystostomy or ureteroureterostomy. Careful post-operative surveillance with pyelograms is indicated to detect persisting obstruction in cases in which ureterolysis has been performed. In case 4, where the level of the obstruction lay in mid pelvis, the " psoas hitch " manœuvre, described by Turner-Warwick and Worth (1969), was found to be particularly applicable in bridging the ureteric defect.

In the unusual event of the diagnosis of unilateral obstruction of the ureter from endometriosis being established without operation, a trial of the modern progestogenic treatment of endometriosis may be justified with serial pyelograms.

SUMMARY

The clinicopathological features of 5 cases of endometriosis of the ureter are presented including an example of bilateral ureteric involvement and carcinomatous change in another. The difficulties in diagnosis and surgical management are discussed and it is suggested that the surgical procedure of choice is ureteroneocystostomy.

The authors are grateful to Professor S. G. Clayton, Mr D. A. Packham and Mr M. T. Rosenberg for permission to publish details of their cases, and also to Professor S. G. Clayton for his advice in the presentation of this paper.

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THE CALIBRE OF THE ADULT FEMALE URETHRA

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Epidemiological studies of complete populations in recent years (Waters *et al.*, 1970) have shown that almost every woman will experience urinary frequency and dysuria at some time in her life. A few of these episodes will be considered severe enough for the woman to consult her general practitioner and only a small proportion of these will be referred to a urologist. Even so, these women make up at least 30 per cent of adult female out-patient referrals and may also pose considerable problems in successful management.

Only a few of these patients are found to have significant urinary or vaginal infections, and so the term " Urethral Syndrome " has been preferred to the incorrect diagnosis of cystitis. The ætiology of this symptom-complex is disputed, but by far the most popular view holds that obstruction in some form is present at the bladder-neck or beyond. For the past 40 years the literature has abounded with articles urging the urologist to search for and treat obstruction. Unfortunately, objective evidence for bladder-neck obstruction or distal urethral stenosis or meatal stenosis in these patients has not been particularly convincing, mainly because comparison with normal subjects has almost always been lacking. Despite this, the most commonly performed treatment is urethral dilatation, though Kunin (1969) has remarked to urologists: ". . . if dilatation of the urethra were a drug, you would not be able to market it without some data to indicate efficacy ". Although various reports (for example, Davis, 1956; Roberts and Smith, 1968) have shown symptomatic improvement following dilatation to occur in up to 80 per cent of cases, none has been controlled to assess the placebo effect, which in studies in other fields has been shown to produce almost equal success rates (*British Medical Journal*, 1970).

As well as the lack of control studies, there is a surprising dearth of information about the range of urethral calibre that is found in the normal healthy adult woman. A search of the English-language urological literature (assisted by Medlars) has revealed no adequate evidence, although 2 valuable studies have been made on normal young girls (Graham *et al.*, 1967; Immergut *et al.*, 1967). One paper considered that a calibre of 22 Ch. was pathological, but offered no evidence in support of the statement (Roberts and Smith, 1968). Mitchell and Hamilton (1964) state that ". . . the normal calibre averages 8 mm." (24 Ch.), but again do not give the range of normals or any evidence. A rational treatment policy is, of course, impossible if the findings in a particular patient cannot be compared with a *true* range of normal values.

Method.—In the present investigation only the distal urethral segment or the external urinary meatus have been measured; there are 2 reasons for this. First, there is abundant evidence (Shopfner, 1970; Lyon and Tanagho, 1965) that this is structurally and functionally the least distensible part of the female urethra and during voiding is always the narrowest segment. Second, this is the only part of the urethra that the endoscopist can calibrate either with sounds or with the trial passage of a cystoscope.

Conventional bougies with their gradual taper can easily exert considerable radial force far in excess of that occurring during voiding, thus making calibration inaccurate. The Otis conical bougies, on the other hand, do not have this effect. Beginning with small sizes, the well-lubricated bougies are passed gently along the urethra and withdrawn in the direction of urine flow. No resistance is felt until on withdrawing one bougie a " catch " is felt as the shoulder of the instrument is drawn through the distal segment, and at the same time the external meatus is usually seen to be slightly tented-up over the bougie. The next size of bougie (2 Ch. larger) almost always fails to pass easily into the meatus thus confirming the calibration point. The calibre of the smallest bougie which encounters definite resistance on being withdrawn in the direction of urine flow is therefore taken to indicate urethral calibre. This measurement is simple, is readily reproducible and was chosen because it seemed to mimic most accurately the distension of the urethra caused by the urinary stream during voiding.

Two groups of patients have been compared.

Group A: Patients without Symptoms.—Women about to undergo minor gynæcological surgery under general anæsthesia were interviewed. Permission for urethral calibration was obtained after the procedure was explained (4 per cent refused) and patients were selected if:

they were between 17 and 45 years of age;
they were not pregnant nor less than 6 months post-partum;
they had never had an indwelling urethral catheter;
they denied any urinary symptoms whatsoever during the preceding 3 months.

If on direct questioning they admitted to any dysuria, or diurnal frequency worse than 2-hourly, they were excluded.

Group B: Patients with Symptoms.—The same criteria were used to select at random women undergoing cystoscopic investigation under general anæsthesia in this department, *except* that these patients had had *both* urinary frequency and dysuria on 1 or more days during the preceding 3 months. If the cystoscopic specimen of urine was infected or a macroscopic bladder lesion (*e.g.* bladder tumour or stone) was found, the patient was excluded from the study.

All interviews and measurements were carried out by the writer.

TABLE I

Age (years)	17-25	-35	-45	Totals
Group A (no symptoms)	10	20	7	37
Group B (with symptoms)	8	9	9	26

$\chi^2 = 2{\cdot}793$; $n = 2$; $0{\cdot}3 > P > 0{\cdot}2$.

TABLE II

Parity	0	1 or 2	3 or more
Group A	14	12	11
Group B	12	10	4

$\chi^2 = 1{\cdot}749$; $n = 2$; $0{\cdot}5 > P > 0{\cdot}3$.

TABLE III

Calibre (Charriere)	A $\leqslant 18$	B 20	C 22	D 24	E $\geqslant 26$
Group A	4	7	7	3	16
Group B	5	1	5	6	9

Grouping columns A with B and C with D gives:
$\chi^2 = 1{\cdot}608$; $n = 2$; $0{\cdot}5 > P > 0{\cdot}3$.

Results.—Tables I and II compare the 2 groups and show that in respect of *age* and *parity* the difference is no greater than would be expected to occur by chance when sampling the same population on 1 out of 3 occasions. Table III shows that in respect of urethral calibre also, the 2 groups are significantly similar.

DISCUSSION

These findings suggest that meatal or distal urethral calibre is highly unlikely to be a factor in producing the 2 symptoms of urinary frequency and dysuria. As evidence is now accumulating (Scott *et al.*, 1966) that urethral resistance or obstruction is almost always produced entirely in this segment, there is reason to doubt whether the *apparent* efficacy of urethral dilatation is due to its effect on obstruction, or whether it may act in some other way. Two other hypotheses have been advanced: that dilatation acts by improving the drainage of congested paraurethral ducts, or that it relieves urethral spasm. The assessment of the progress of the urethral syndrome depends upon the patient reporting the frequency and severity of relapses, for characteristically the symptoms are intermittent. These purely subjective findings are very likely to be influenced by both suggestion and the reassurance of the absence of serious disease that a cystoscopic examination gives. Any valid trial of treatment should therefore be carefully controlled to exclude this factor by double-blind techniques.

This study also shows that a distal urethral calibre of 20 Ch. or less is a normal finding in about 30 per cent (11 of 37) women who do not have the symptoms of the urethral syndrome. This means that the diagnosis of meatal stenosis (which tends to imply a stricture causing symptoms) should be made with care and only very rarely.

I am pleased to thank Professor John Swinney, Mr Linton Snaith and the staff of the Departments of Urology and Gynæcology, Newcastle General Hospital, for allowing me to investigate their patients, and also Mr R. A. McNay, Statistician, and Mr W. Keith Yeates for their helpful criticism during the preparation of this paper.

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SIMPLE RENAL CYSTS IN CHILDHOOD

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The origin and nature of retro-peritoneal masses in childhood may be difficult to ascertain clinically and after radiological investigations. Very often, a malignant lesion may be diagnosed, nephroblastoma and neuroblastoma being fairly common.

Non-malignant renal conditions such as hydronephrosis or pyonephrosis, renal duplications and renal cysts may also present as abdominal masses. Whereas infantile polycystic and multicystic kidney disease are well-recognised entities, simple renal cysts are not usually encountered in the pædiatric age-group. Numerous large series have however been reported in adults (Kropp *et al.*, 1967; Gernert *et al.*, 1968; Hale and Naunton Morgan, 1969; Notley and Williams, 1969).

In this paper the clinical and radiological features, operative findings and differential diagnosis in two cases of simple renal cysts in childhood are discussed. Both patients presented with symptom-free abdominal masses.

CASE REPORTS

Case 1.—W. R., a 6-week-old female baby, was admitted to another hospital with pneumonia when a mass was also noticed in the right loin. After treatment of the pneumonia she was transferred to Royal Manchester Children's Hospital for investigation and surgical treatment. The only positive finding was a large, firm, smooth right loin mass which was seen clearly on plain X-ray of the abdomen (Fig. 1). Intravenous pyelogram showed downward and medial displacement of the right kidney. Catecholamine excretion was normal and nephroblastoma was diagnosed.

On 12th December 1967 laparotomy was performed through a transverse upper abdominal incision. The right kidney was exposed and was found to contain a cyst arising from its upper pole. The cyst was 10 cm. in diameter, was separate from the right adrenal gland and did not communicate with the right pelvi-calyceal system. The cyst contained clear fluid and was excised. Post-operative recovery was uneventful and a follow-up pyelogram was satisfactory. Histology showed a cyst with a fibro-elastic wall and an epithelial lining.

Case 2.—Y. P., a 9-year-old Pakistani girl, was admitted to Royal Manchester Children's Hospital with an asymptomatic left upper quadrant mass, discovered by the school doctor on routine examination. Clinically a large mass was found to occupy the left hypochondrium with a loop of colon lying across it. The mass was uniformly smooth and was considered cystic by some observers. Diagnosis between a benign cystic or a malignant lesion on the one hand and between a renal or a splenic lesion on the other, was strongly debated.

Laboratory investigations; Hb. 11·0 g. per 100 ml.; W.B.C. 3,800 per c.mm. with neutrophils 47 per cent; lymphocytes 50 per cent; monocytes 1 per cent and eosinophils 2 per cent; platelets 290,000 per c.mm.; erythrocyte sedimentation rate 10 mm. in 1 hour (Westergren); serum electrolytes, urea, proteins, liver function tests and catecholamine excretion normal; Casoni test negative; urinalysis normal.

Radiological investigations (Figs 2-5): X-ray of chest normal; X-ray of abdomen showed an enormous soft tissue mass in the left upper abdomen with downward and medial displacement of the left kidney on intravenous pyelogram; barium meal showed displacement of the stomach to the right; an aortogram showed an avascular mass displacing the splenic artery upwards and the left kidney downwards and medially. These findings were consistent with the diagnosis of a cystic mass which was thought to be arising from the left kidney or possibly the spleen. Percutaneous needle puncture was performed (immediately preceding laparotomy) and clear watery fluid was obtained from the cyst, which was delineated by instillation of contrast medium.

Laparotomy was performed through a transverse upper abdominal incision on 23rd June 1970. A large cyst, 16 cm. in diameter, occupied the upper half of the left kidney but did not communicate with its pelvi-calyceal system. The cyst was dissected off the kidney, leaving a raw renal area and an opening in the renal pelvis. As the kidney was very mobile it was fixed and tube nephrostomy performed. The child made a good post-operative recovery. A nephrostogram was performed a week after operation (Fig. 6) and the tube removed soon afterwards. Pathological examination showed a unilocular cyst with an epithelial lining.

FIG. 1

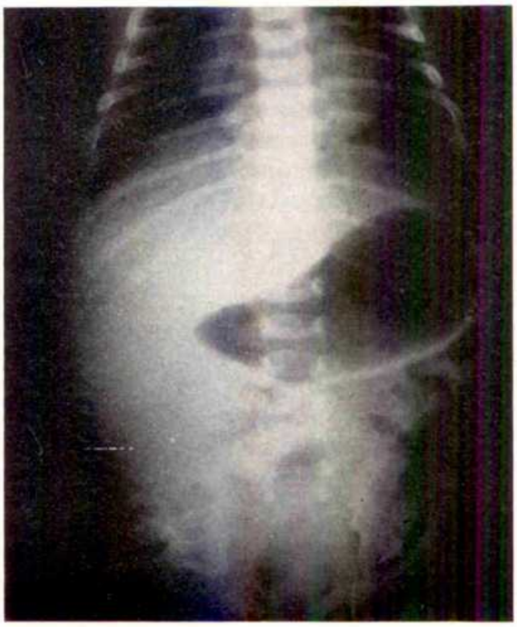
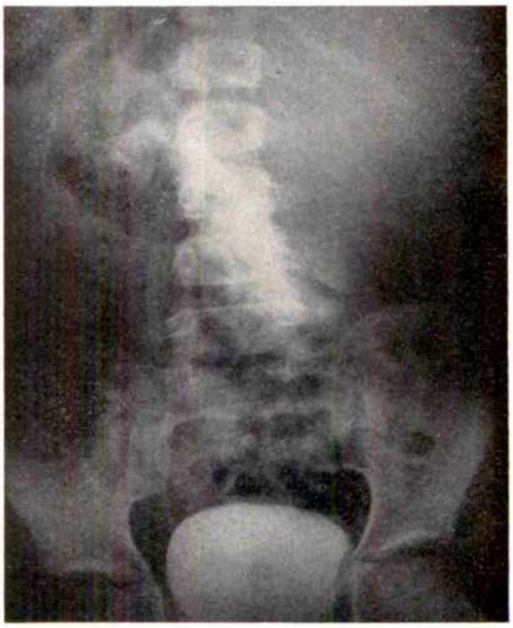


FIG. 2



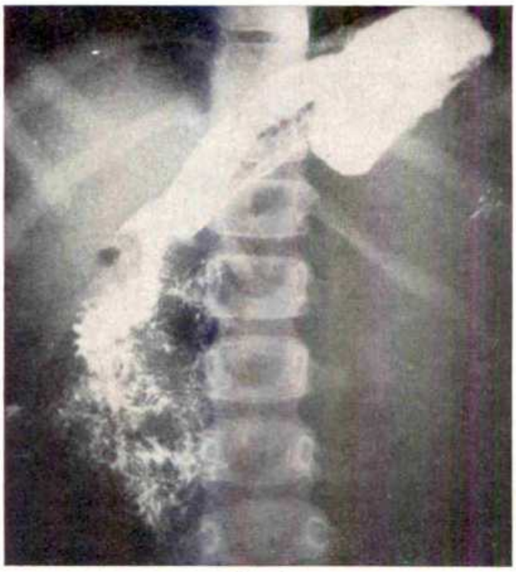


FIG. 3

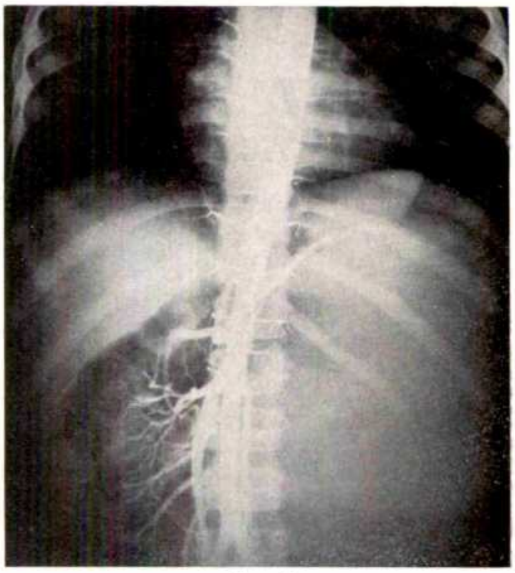


FIG. 4

Fig. 1.—Case 1. Plain X-ray abdomen showing an obvious soft tissue mass in the right upper abdomen. There is no calcification.

Fig. 2.—Case 2. Intravenous pyelogram showing a normal right kidney. There is downward and medial displacement of a hydronephrotic left kidney by an enormous soft tissue mass.

Fig. 3.—Case 2. Barium meal showing the stomach to be displaced upwards and to the right along with the proximal small bowel.

Fig. 4.—Case 2. Aortogram showing an avascular mass in the left side. Note the splenic artery stretched over the superior aspect of the mass and the left renal artery pushed downwards and medially.

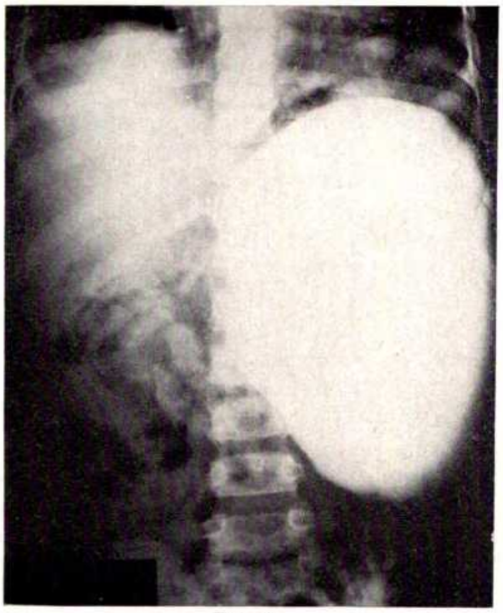


FIG. 5

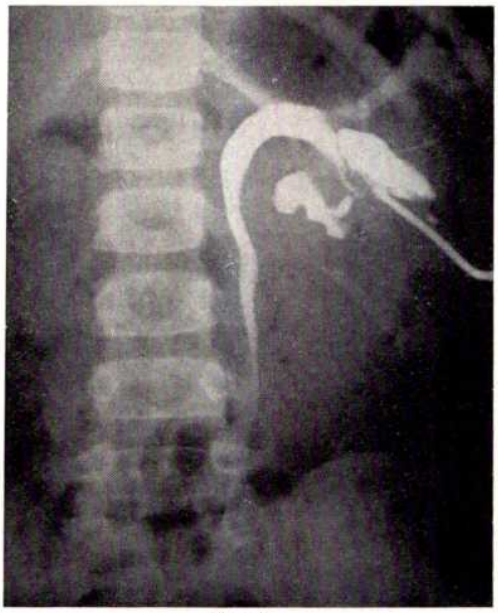


FIG. 6

Fig. 5.—Case 2. Renal cystogram after percutaneous puncture showing extent of the cystic mass in the left upper quadrant.

Fig. 6.—Case 2. Nephrostogram, 1 week after operation, showing the residual hydronephrotic kidney with normal ureter.

DISCUSSION

In case 1, the presence of a right loin mass causing renal displacement without calcification and with normal catecholamine excretion favoured the diagnosis of a renal tumour and surgical exploration was mandatory.

In case 2, after investigations had been completed, it was obvious that the diagnosis was that of a cystic space-occupying lesion in the left upper abdomen, causing left renal and gastric displacement. Differential diagnosis was between a cyst arising from the left kidney or the spleen but a left upper quadrant cyst could also take origin from the left adrenal, pancreas or left lobe of the liver.

Adrenal cysts are rare but have been described in childhood (Van De Water and Fonkalsrud, 1966). The pyelographic appearances were against this diagnosis as an adrenal cyst is usually separate from the kidney, which is displaced downwards and laterally.

In the absence of a history of trauma or pancreatitis, pancreatic pseudocyst seemed unlikely (Bongiovi and Logosso, 1969). Barium studies were against the diagnosis of a true pancreatic cyst, a rare condition in childhood or a pancreatic pseudocyst. In both conditions there is usually anterolateral or superior displacement of the stomach or widening of the duodenal loop (Grossman and Redo, 1966; Gundersen and Janis, 1969).

A cyst arising from the left lobe of the liver was considered unlikely; apart from being very rare, it characteristically displaces the stomach to the left with normal appearances on intravenous pyelogram (Grossman and Redo, 1966).

A cyst of the spleen was considered a possible diagnosis. The presence of a left upper quadrant mass with radiological demonstration of gastric and renal displacement in an otherwise healthy girl favoured this diagnosis (McNamara *et al.*, 1968). The position of the colon lying across the cyst, however, was against this diagnosis, as a cyst of the spleen characteristically displaces the colon downwards (Gandhi and Bain, 1962).

Renal cysts are relatively uncommon in infancy and childhood. The lack of clear definitions of various types of cysts that may be encountered has caused considerable confusion in terminology. The various clinical, pathological and radiological characteristics of renal cysts in childhood have been considered in detail by Gwinn and Landing (1968).

Simple or serous cysts of the kidney arise from the renal cortex. Usually there is a single cyst in the upper or lower pole, but there may be 2 or 3 cysts in one kidney. Deweerd and Simon (1956) reviewed 21 cases of simple renal cysts in childhood, including 5 of their own cases. Gall and Kurtz (1958) reported another case, and the 2 cases described here bring the total number of cases of simple renal cysts reported in childhood to 24. Deweerd and Simon (1956) stressed various criteria for the diagnosis of simple renal cysts which are fulfilled by the 2 cases under review.

The cysts were unilocular, were lined by epithelium, they did not communicate with the renal pelvi-calyceal system and the renal pelvis and ureter were normal.

The presenting complaint in most of the previously recorded cases in childhood was that of an abdominal mass with few associated symptoms. The mass was completely asymptomatic in both cases reported in this paper. In contrast, in a large proportion of the adult patients with simple renal cysts urological or other symptoms were present.

The diagnosis of a simple renal cyst can be made by conventional urological investigations together with nephrotomography, renal angiography and renal cystogram after percutaneous puncture (Woodruff *et al.*, 1956). Percutaneous puncture and aspiration of the cyst has also been used as a therapeutic measure in adults rendering surgical exploration unnecessary (Wahlquivst and Grumstedt, 1966). It would appear that this form of treatment should be reserved only for the poor-risk patient (Clarke *et al.*, 1956) and is certainly not recommended in childhood. The inherent danger of missing a renal neoplasm, a much commoner condition in childhood, must be high. Even when the cystic nature of the mass is obvious, definitive surgical intervention rather than needle aspiration is more likely to prevent deterioration and destruction of the kidney.

Therefore, in all cases in childhood, the kidney should be explored with excision of the cyst and preservation of the residual kidney. This may not always be possible, as in 12 of the previously reported cases, nephrectomy was actually performed.

SUMMARY

Two cases of simple renal cysts, a rare condition in childhood, are described. Clinical presentation was of a symptom-free abdominal mass which was interpreted as a renal neoplasm in the first case. In the second case it was suspected that the mass was cystic and this was affirmed by radiological investigations. Differential diagnosis of a left upper abdominal cystic mass in childhood is discussed. In both cases the cyst was well demarcated from the adjoining parenchyma and was resected without sacrificing the kidney.

I wish to thank Mr A. Jolleys and Mr S. J. Cohen for permission to report the cases and Mr Nicholls for the illustrations.

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SIMPLIFIED RENAL HYPOTHERMIA: AN ADJUNCT TO CONSERVATIVE RENAL SURGERY[1]

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HYPOTHERMIA of the surgically exposed kidney is now recognised as being practical, beneficial and safe and allows the surgeon to clamp the renal artery for an extended period and ensure against the effects of long-term renal ischæmia. To the surgeon the advantages of renal arterial occlusion are obvious. Renal tissue turgor is reduced so that calculi or intrarenal abnormalities are more readily palpable and it becomes possible to incise, explore and reconstruct the calyceal system of the kidney without fear of excessive blood loss.

In the field of conservative renal surgery (Wilson, 1963; Smith and Boyce, 1968; Hanley *et al.*, 1968) renal transplantation (Crouch *et al.*, 1965; Martin *et al.*, 1970) and more recently amongst those workers interested in the maintenance of extracorporeal renal perfusion (Humphries *et al.*, 1968; Van Zyl *et al.*, 1968; Olsson *et al.*, 1969) it has been conclusively demonstrated that the experimental and human kidney can tolerate long periods of total ischæmia and return to normal function if hypothermically maintained throughout the ischæmic phase.

The aim of hypothermia must be to reduce cellular metabolic activity so that the cells of the renal parenchyma will tolerate a period of total ischæmia. This particularly applies to the cells of the proximal convoluted tubules which Oliver *et al.* (1951) and Rama Jaju *et al.* (1969) have demonstrated to be most susceptible to ischæmia. A further aim must be to inhibit the formation and build up of destructive autolytic enzymes normally produced and allowed to accumulate in ischæmic tissue. Levy in 1959 and Walter and Bright in 1967 demonstrated that reduction in renal parenchymal temperature of 10° diminished cellular respiration by 75 per cent, a 20° fall in temperature further reduced the oxygen consumption to 85 per cent of normal while at a tissue temperature of 7°C 93 per cent of respiration was inhibited.

Hoffman, Burger and Persky showed in 1965 that the canine kidney can be isolated and maintained at 5°C for 24 hours and can support life and apparently function normally when re-implanted. Martin, Smith and Fareed in 1970 indicated that hypothermia alone was the best way of preserving renal function in kidneys maintained extracorporeally for 8 hours and compared organs that had been preserved by surface coolant at 5°C with others that had been perfused by cooled plasma and a variety of electrolyte solutions.

The clinical experience of Hanley *et al.* (1968), and Wilson in 1963 has demonstrated the practical application of hypothermia to conservative renal surgery. It is significant that in all reported series where hypothermia has been applied in the clinical situation no serious long-term renal complications have developed as a result of cooling. This fact has been verified by our own experience with slush cooling.

Materials and Methods.—Sterile slush is packed around the exposed kidney and confined within a rubber dam for the duration of the operative procedure.

Patients.—In the last 10 years at North Carolina Baptist Hospital, more than 300 patients have been subjected to local renal hypothermia. Since the technique of cooling was adopted as a routine operating-room procedure for all kidneys undergoing segmental surgery with total ischæmia, precise records have not been kept, but a retrospective study of available records indicates that more than 34 patients a year in the period 1960 to 1969 have been subjected to regional hypothermia with slush cooling. Table I indicates the breakdown of causes for surgical intervention.

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[1] Supported in part by The John A. Hartford Foundation, Inc.

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TABLE I

1. Renal nephrolithiasis	75%
2. Renal arterial disease	15%
3. Segmental resection for local infection of benign tumour	10%

TABLE II

CONSTITUENTS OF PHYSIOLOGICAL IRRIGATING SOLUTION*

Each 100 ml. contains:

Sodium Chloride U.S.P.	800 mg.
Hydrous Dextrose U.S.P.	100 mg.
Potassium Chloride U.S.P.	40 mg.
Magnesium Sulfate U.S.P.	20 mg.
Dibasic Sodium Phosphate Heptahydrate	8.7 mg.
Monobasic Potassium Phosphate	6.2 mg.
Water for Injection U.S.P.	q.s.

Concentration of Electrolytes (mEq./L):

Sodium	138 mEq./L
Potassium	6 mEq./L
Magnesium	2 mEq./L
Chloride	142 mEq./L
Phosphate	1 mEq./L
Sulfate	2 mEq./L

*Commercially prepared by McGaw Laboratories and Trauanol(Tissusol)

The Slush.—This is the name given to the soft ice formed by the freezing of physiological irrigating fluid. This is a commercially synthesised ultrafiltrate of plasma prepared as a sterile solution and made available in litre glass containers with a wide mouth to facilitate easy emptying of the formed slush. Table II indicates the constituents of this solution.

Slush is formed by freezing this fluid in the freezing compartment of a conventional domestic refrigerator. The process, if the container is initially at room temperature, takes approximately 4 hours. In the final 2 hours each bottle is shaken vigorously every 20 to 30 minutes to ensure that the ice formed is produced in small, soft crystals. The physiological solution particularly lends itself to the formation of this form of ice. Once the crystals have become obvious, the further freezing process is rapid. For each operative procedure 10 bottles are prepared, of which 5 or 6 usually suffice. In this unit 10 bottles are continually kept refrigerated and the subsequent freezing process can be accomplished in 90 minutes even without using fast freezing processors.

The Dam.—This is formed by an 18″ × 24″ rectangular latex rubber sheet with a 9″ cut on one long border which is parallel to and equidistant from either end. The cut surfaces pass to either side of the structures of the dissected renal hilum and centrally are gathered firmly about the hilum and clamped with a bulldog or Kelly clamp. The rest of the cut surfaces are rolled together to form a water-tight seal and are clamped at variable distances along their length.

Temperature Control.—Renal core and peripheral temperatures have been monitored using a Yellow Springs telethermometer with a needle thermocouple temperature probe. From these studies curves were drawn to indicate the rate of cooling, the temperature gradient within the kidney at any one time and the rate of warming relative to the increase in renal blood flow monitored with a square wave electromagnetic flow meter. From these determinations composite charts were developed (see Figs. 1-3). Subsequent studies have verified the accuracy of these curves and have shown that both cooling and rewarming phases as well as the renal temperature gradient is remarkably constant and can be predicted using the curve and knowing the time of renal ischæmia and onset of cooling. The charts also compare favourably with the temperature-time relationship of other series. Apart from verifying these charts or assessing core and peripheral temperatures in long procedures we do not, as a routine, monitor renal parenchymal tissue temperatures and the temperature probe is not considered an indispensable part of the technique.

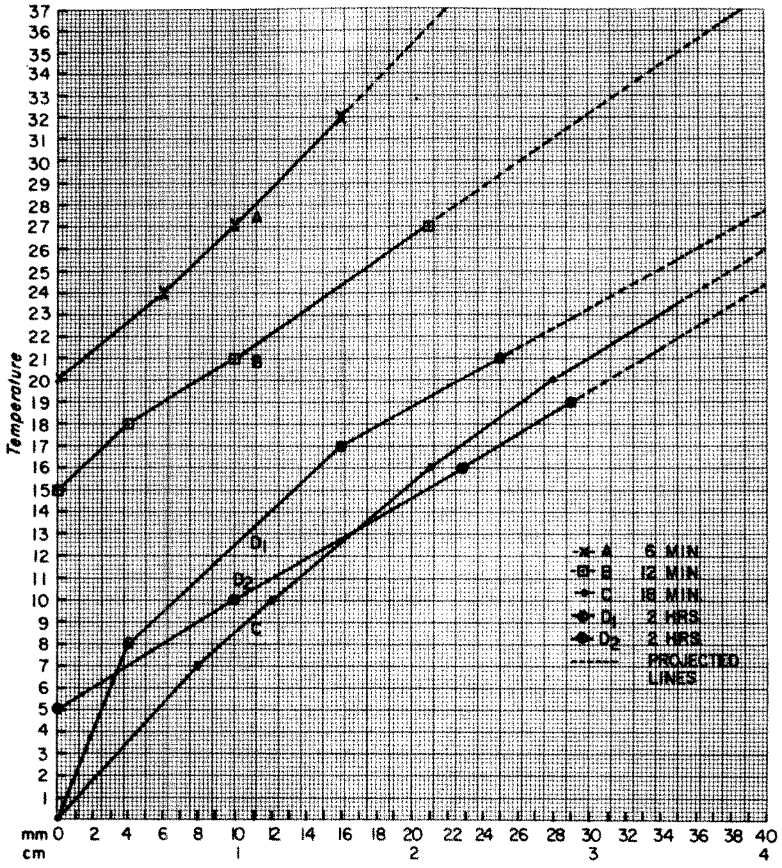


FIG. 1

A time-integrated renal temperature depth chart.

Method.—The kidney is surgically exposed and freed and the renal artery dissected free from the hilar structures. Separate tapes are usually employed to suspend the kidney from either pole and isolate the dissected renal artery for easy identification (Fig. 4).

The rubber dam is then placed *in situ* and abdominal packs insulate it from the rest of the operative wound. A clamp is placed on the renal artery, slush is packed around the kidney

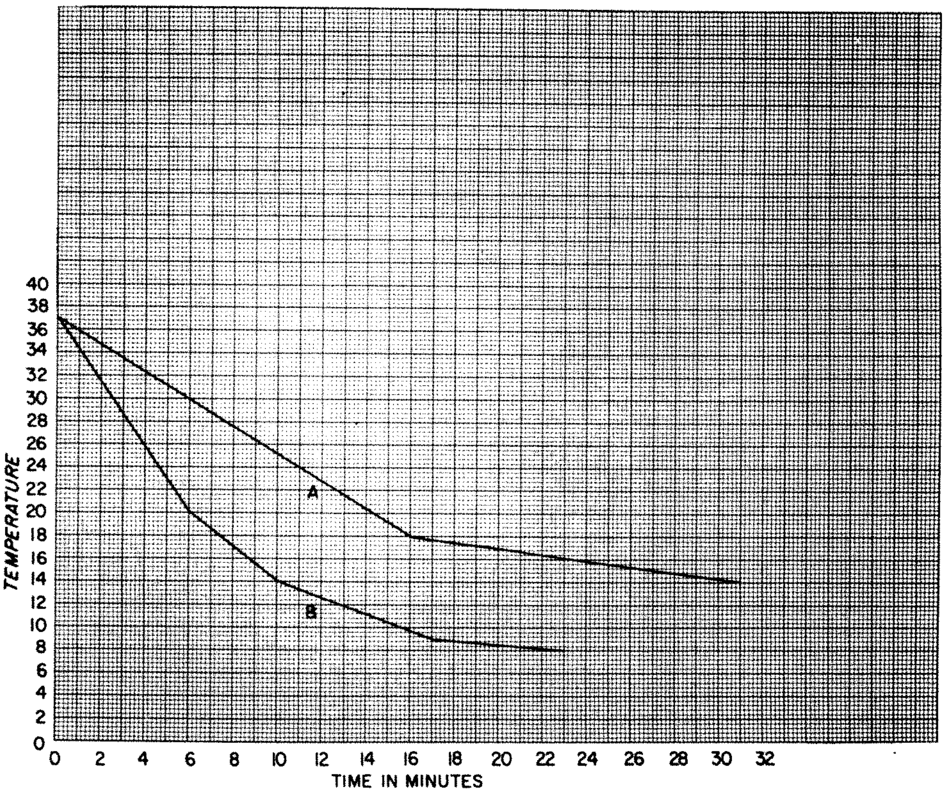


FIG. 2

Temperature-time relationship for a kidney cooled during renal arterial endarterectomy and by-pass grafting. A, Core temperature. B, Peripheral temperature.

confined within the dam and the operation proceeds (Fig. 5). Peripheral temperature is rapidly reduced closely followed by core temperature. This effect is further enhanced should a nephrotomy be performed in the course of the operative procedure and slush is allowed to enter the renal collecting system. A surgical sucker is used to remove dissolved slush from within the kidney or the dam site and this is replaced from a bowl of slush ice maintained in readiness by the scrub nurse. One assistant is designated to maintain the slush in contact with the kidney throughout the procedure and to apply suction as necessary. At the completion of the procedure slush is removed from around the kidney and if necessary can be replaced by warm saline to enhance warming. Once the slush is removed the clamp is released from the renal artery.

DISCUSSION

This method differs from other clinical applications of regional hypothermia in that the cooling process is maintained throughout the procedure and " ischæmic time " is not lost in waiting for basal temperatures or in the recooling of the previously cooled kidney that has warmed in the course of a long procedure.

Wilson reported 22 cases in which he had used sterile ice packed around the kidney to produce hypothermia and accepted 15 minutes as the average period to achieve a core temperature of 20°C. His method is similar to others that require the removal of coolant prior to the com-

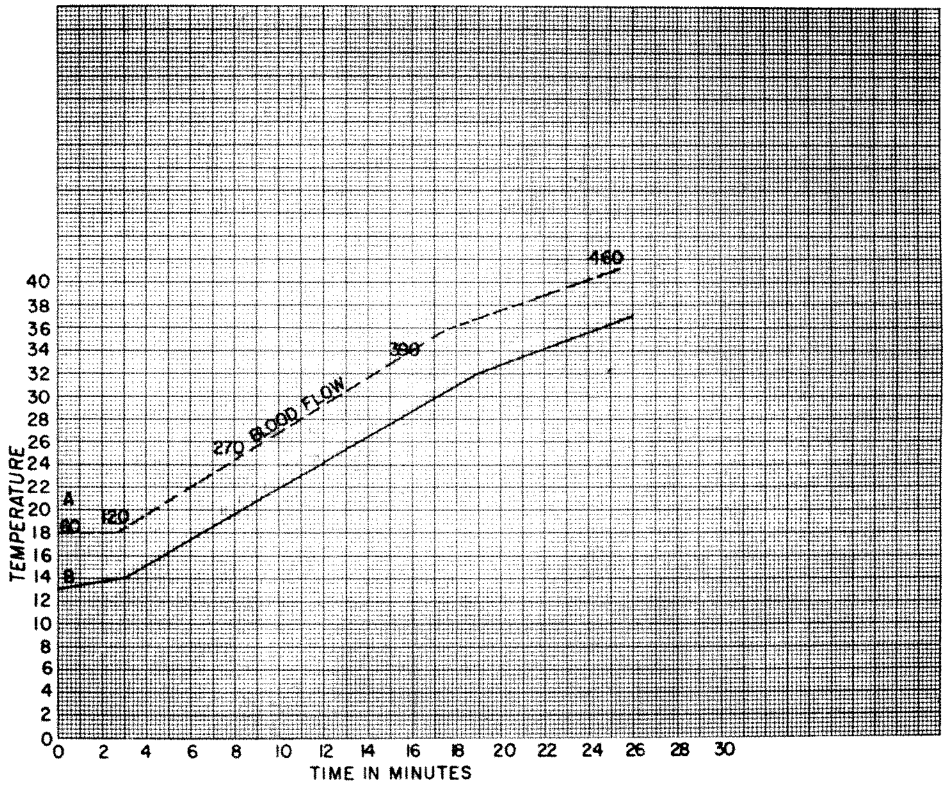


FIG. 3

Temperature-time relationship for core temperature during unassisted rewarming. Alteration of renal blood flow is superimposed.

mencement of surgery and Wilson admits that in some cases recooling was necessary. A similar method was advocated by Graves in 1963 while Cockett in 1961 developed a bivalved heat exchanger to surround the kidney. These methods appear to be effective although still requiring an ischæmic period of surgical inactivity while cooling to the required core temperature is obtained. Hanley, using a pump to circulate precooled alcohol at 7°C through latex rubber cups, was able to reduce this time to less than 10 minutes, but, at the expense of simplicity, he offered an effective but more complex system for regional hypothermia. As Figures 1 and 2 indicate cooling to a core temperature of 20°C takes an average of 15 minutes using slush cooling techniques, but one must consider that the average ischæmic time for nephrotomy and plastic repair of the calyces (performed for 80 per cent of intrarenal stones removed at North Carolina Baptist Hospital) is 45 minutes and realise that this procedure is already one-third completed before other methods would allow the surgeon to commence.

How Important is Renal Ischæmic Time under Hypothermic Conditions?—Experimentally Wickham *et al.* (1967) demonstrated that rabbit kidneys showed little deterioration of function after 3 hours of cooling, but more marked damage after 4 hours of hypothermic ischæmia. They further demonstrated that in the human kidney 84 minutes of renal ischæmia at 20°C failed to produce any permanent depression of renal function. Wilson reported ischæmic periods up to 134 minutes in his series without long-term effect. In this present series the longest period of ischæmia was 190 minutes in a technically difficult renal arterial correction. The great majority

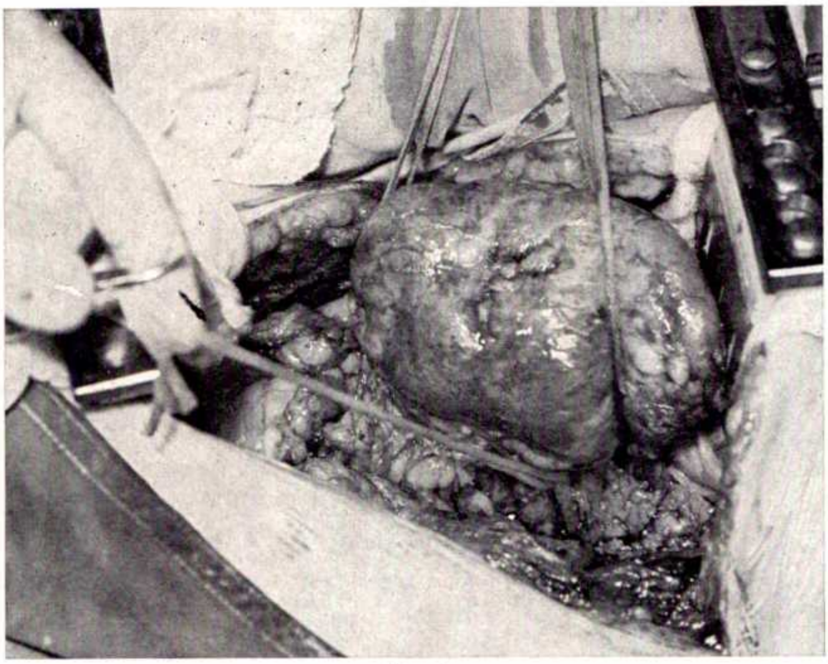


FIG. 4

A kidney prior to cooling. Note the use of tapes to suspend the kidney and allow rapid identification of the renal artery.

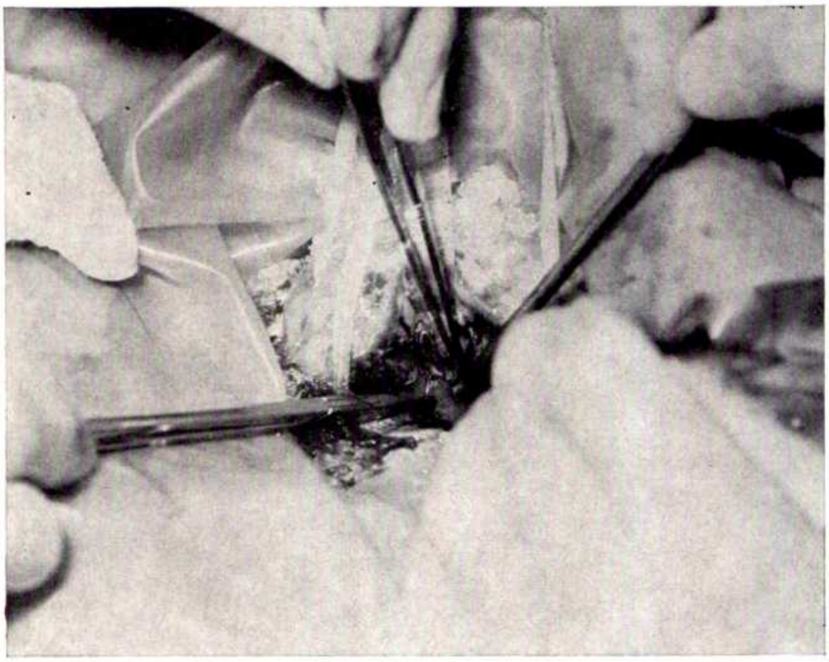
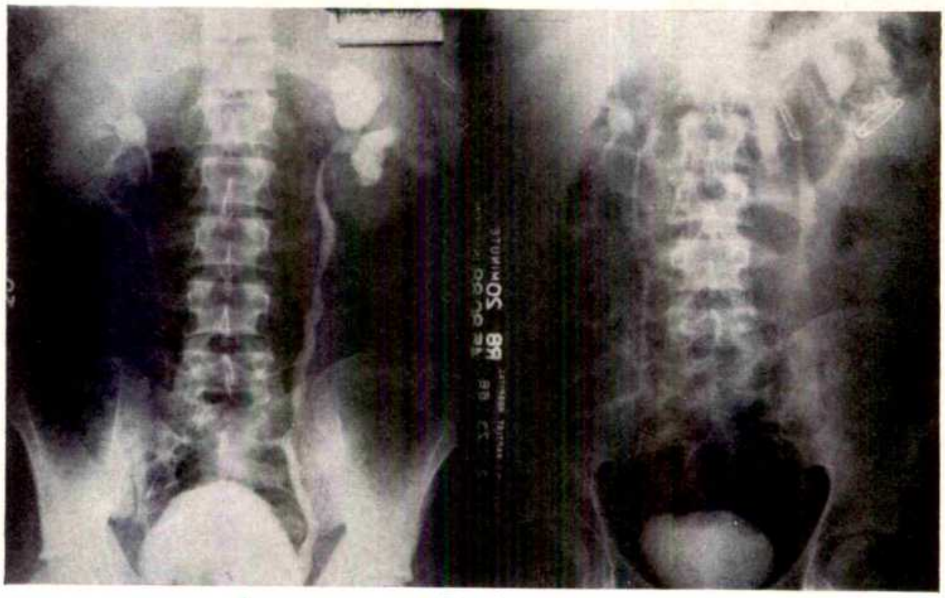


FIG. 5

Intrapelvic reconstruction of an incised and opened calyceal infundibulum. Note the kidney within the rubber dam, the slush-ice, and the absence of bleeding in the operative field.



A FIG. 6 B

Two 20-minute intravenous pyelograms of the same patient. A, 24 hours prior to surgery showing an intrapelvic staghorn calculus with obstruction to urinary outflow. B, 24 hours after anatrophic nephrolithotomy showing equal excretion of contrast by the two kidneys.

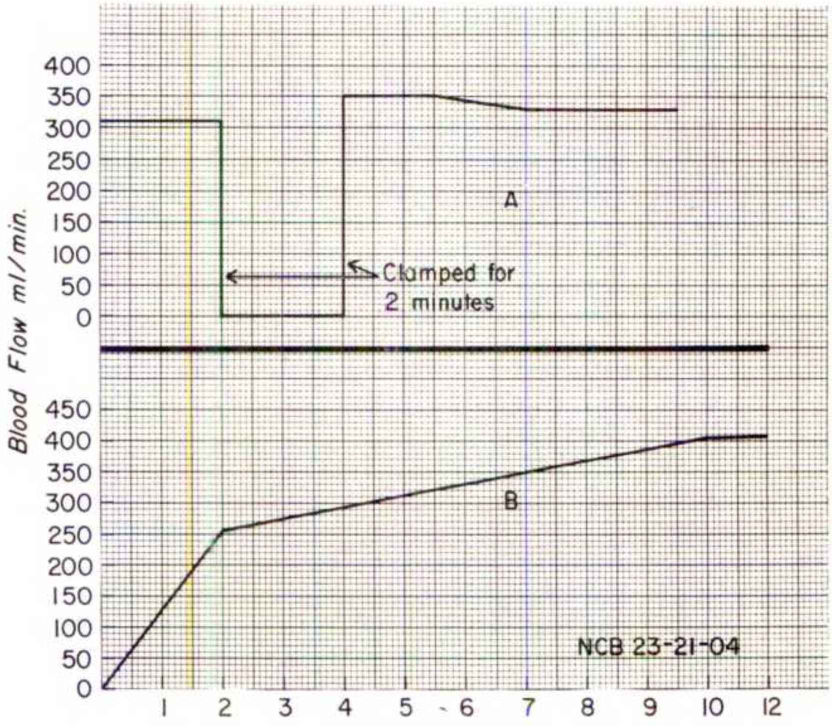


FIG. 7

Renal arterial flow studies on a kidney operated on for a staghorn calculus (slush cooling). A, Prior to arterial clamping—demonstrating post-ischæmic hyperæmia. B, Post-arterial clamping—rewarming phase (assisted with warm saline).

of our cases do not have an ischæmic time greater than 60 minutes and many are for shorter periods.

No immediate tests of renal function are performed to demonstrate renal impairment as a result of cooling. It should be stressed that the patients requiring this specialised treatment often present with multiple stones or staghorn calculi, with urine grossly infected with resistant bacterial organisms and having frequently sustained previous surgical procedures on one or both kidneys. A number in our series have had staghorn calculi removed from their only kidney while others have required nephrolithotomy for staghorn calculi of both kidneys at separate procedures. Any deterioration in renal function in this group must logically result as much from the surgical insult as the cooling procedure, and although serum electrolyte and renal clearance estimations are routine in the post-operative period, they are assessed only as an overall measure of renal function and have not been subjected to analytical study to determine any component resulting from renal hypothermia. Intravenous urograms performed within 24 hours after surgery (Fig. 6) demonstrate equal excretion of dye initially and comparable concentration of dye in the collecting systems in later films. Renograms and selective radioactive technesium renal clearance studies in the immediate pre-operative and post-operative periods have also been performed and have failed to demonstrate any gross deleterious effect of hypothermia.

Long-term follow up of a selected group of 36 patients, with renal clearance studies and fluorography, has been previously reported (Smith and Boyce, 1967) and these studies failed to indicate any deterioration in renal function as a result of either the operation or the cooling process.

The measurement of renal blood flow has been recorded both in the pre-ischæmic phase and following the release of arterial clamping. Figure 7 demonstrates the increase in renal blood flow following left nephrolithotomy under hypothermic conditions in a 60-year-old man with bilateral renal stone disease. The left kidney had sustained previous operative procedures for the removal of stones while the right kidney had been operated on once previously. Cultures indicated the urine to be grossly infected with resistant organisms.

One can speculate on the reason for the increase in renal blood flow following the removal of stones. Certainly one factor must be a decrease in the resistance to outflow of urine from the renal tubules, and at least it becomes obvious that neither the operative procedure nor hypothermia has increased intravascular resistance and diminished renal arterial flow.

In answer to the previously posed question the following aims must be stated. Our aim is to reduce ischæmic and hypothermic time to a minimum but to ensure that the time factor does not interfere with carefully conducted and unhurried renal surgery. In the case of renal stones, both visual and radiological confirmation that all extraneous intrarenal material has been removed is obligatory and an insurance against the recurrence of stone disease and the persistence of intrarenal infection. Such confirmation is pursued relentlessly, regardless of time, and limited only by factors related to the degree of pathology found in the kidney and the anticipated ability of the patient to withstand the surgical procedure.

To what Temperature is the Kidney Cooled?—Most workers aim at a core temperature of 20°C. This value is based on the work of Bickford and Winton (1937), who demonstrated suspended tubular transport function at 15-17°C. Wickham has demonstrated only minor renal functional variation in experimental kidneys following hypothermic temperatures over the range 5°C to 30°C. Little information is available on permanent impairment of renal function in human patients due to low temperature hypothermia.

Figure 1 indicates that the fall in parenchymal temperature is progressive for the first 18 minutes, but after this remains relatively constant so that recordings at 120 minutes show little variation. In renal arterial surgery (Fig. 2) temperatures tend to be lower as the operative field is proximal to the kidney and there is better isolation and insulation of the kidney within the dam. However, relative to stone surgery, the ischæmic time tends to be shorter and excessively low temperatures have not been a problem. Cortical temperatures of less than 5°C are not uncommon and in considering the results of this series we have no cause to believe that cortical function has suffered as a result of these low temperatures.

In favour of continuous cooling is the contention that the degree of metabolic suppression must be directly related to the ischæmic time and it is undesirable to allow renal temperature to rise, with a corresponding elevation of renal metabolic activity, while the cells of the renal parenchyma remain ischæmic.

Wilson reports 1 case which showed a 14°C increase in core temperature during a 60-minute operative procedure, while Hanley indicates an expected rise in core temperature of 10° in 30 minutes. According to Walton and Bryant, at 30°C renal tissue utilises 15 per cent more oxygen than it did at 15°C, and when it is considered that this activity is at the end of a long ischæmic time, when renal cell respiration is never reduced below 15 per cent of total efficiency, there is at least the theoretical possibility of accumulation of metabolic products deleterious to cell membranes.

It should be reiterated at this point that no serious complication has been recorded in our large series of slush coolings, and as time proceeds the additional benefits of this technique become more obvious. These benefits include:

1. The cooling technique allows the surgeon to be in complete control of the hypothermia and not dependent on mechanical appliances or technical staff other than those normally found in an operating room.

2. The technique is especially applicable to those centres where intrarenal segmental surgery is performed infrequently and allows renal cooling without the purchase, storage and maintenance of expensive equipment for occasional use. Because of the simplicity of this technique any surgical unit can take advantage of hypothermia and it facilitates intrarenal surgery with emphasis on the conservation of nephron mass.

3. As reported by Hanley, following hypothermia the incidence of renal hæmorrhage, both immediate, on release of the arterial clamp, and delayed, on reversal of arterial vasoconstriction, is markedly reduced. So consistent is this finding that in this unit nephrostomy tubes have been dispensed with entirely and ureteric silastic stents are used to ensure free urine drainage from the operated kidney. The eradication of infection associated with nephrostomy tubes and persistent nephrostomy tract drainage is apparent in our post-operative patients and has contributed greatly to the rapid improvement and early discharge from the hospital.

SUMMARY

Slush cooling offers a simple technique for regional hypothermia. It is effective, without complications, requires no specialised monitoring equipment and remains efficient for the duration of the operative procedure.

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TREATMENT OF PRIAPISM BY CAVERNO-SAPHENOUS BY-PASS

Case Report

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PRIAPISM is a persistent painful erection not related to sexual stimulation or desire and which, if left untreated, ends in impotence.

Various factors have been found to be responsible for this condition. The better known being sickle-cell anæmia, leukæmia, tumours of the lower urinary tract and trauma. Idiopathic priapism, the commonest form, is the term applied when no underlying cause can be found.

The causes of priapism were well classified by Hinman Jr. (1960) and this classification was extended by Becker and Mitchell in 1965. Characteristically, in idiopathic priapism, the corpora cavernosa alone are involved and are filled with dark thick blood without clots. Refilling with bright red blood occurs after early aspiration, suggesting an impediment to the venous drainage of the corpora.

Various modes of treatment have been employed to cure this condition and have met with varying degrees of success. These methods are either surgical or non-surgical.

Surgical

1. Aspiration and irrigation of corpora cavernosa with heparin.
2. Incision of the tunica albuginea followed by evacuation of blood and reparative suture.
3. Ligation of internal pudendal artery.
4. Caverno-saphenous by-pass.

Non-surgical

1. Sedation.
2. Anæsthesia (spinal, caudal, epidural or general).
3. Curarisation.
4. Anti-androgenic therapy.

What follows is our experience with a case of idiopathic priapism treated by early caverno-saphenous shunt.

Case Report.—Mr J., a 27-year-old white male, presented to the Casualty Department of The Montreal General Hospital with an erection that had not subsided since it had been initiated spontaneously 18 hours previously. He had recently remarried after a 10-year unhappy marriage which ended in a divorce.

He gave no history of painful erections in the past and the present one had only started to become painful 4 hours prior to admission. There had been no loss of appetite or weight and there was no history of venereal disease.

Physical examination revealed a well-built anxious but co-operative man in moderate pain. Physical findings revealed a fully erect phallus with turgid and moderately tender corpora cavernosa. The corpus spongiosum was not turgid. Rectal examination revealed a soft, enlarged prostate that was not tender or fluctuant. Voiding had been spontaneous all along and urinalysis was unremarkable. Liver and spleen were not palpable. Hemogram showed a hæmatocrit of 42, white cell count of 5,400 with a normal differential. Clotting time was 5 minutes and the coagulogram was within normal limits. The diagnosis of idiopathic priapism was made (Fig. 1).

Management.—The ice packs which the patient had already been using before arriving were continued and he was given Demerol 75 mg. i.m., and Heparin (10,000 units) intravenously. Within the next 3 to 4 hours, as no improvement was noted, Valium 10 mg. was administered intravenously in repeated doses. Vigorous prolonged prostatic massage was done. Eight hours following admission the situation was unchanged. The patient was then given Protamine to return the clotting time to normal and continuous epidural anæsthesia was begun. Again no change could be discerned after 6 hours. Accordingly, he was taken to the operating room some 32 hours after the onset of priapism and a left caverno-saphenous by-pass was performed after the technique of Grayhack (Grayhack *et al.*, 1964; Garrett and Rhamy, 1966; Martin *et al.*, 1969; Hamm and Waterhouse, 1970). The procedure consisted in dissecting free the left saphenous vein for a length of 6 inches from the sapheno-femoral junction and ligating its tributaries along the segment. The vein was then divided and injected with a dilute Heparin solution.

FIG. 1

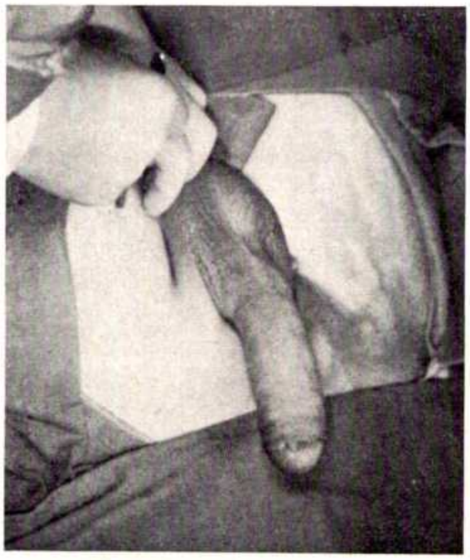
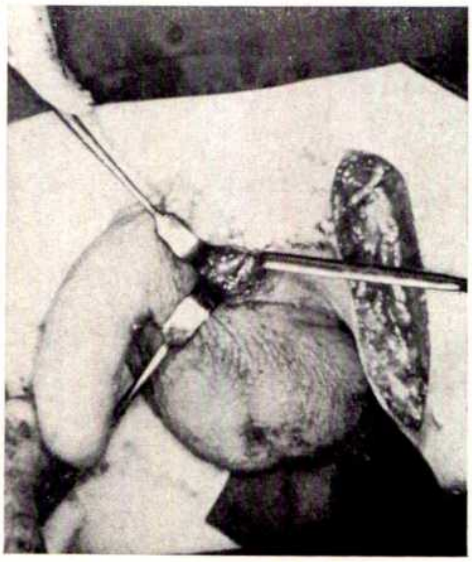


FIG. 2



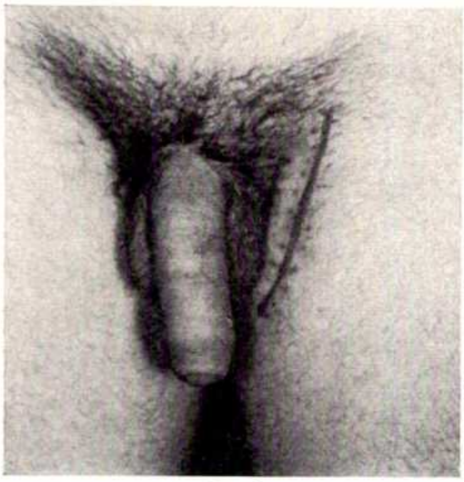


FIG. 3

Fig. 1.—Erect phallus prior to operation.

Fig. 2.—" Corpo-saphenous " shunt in place and functioning well. Note marked subsidence of priapism.

Fig. 3.—Three weeks post-operative. (*Note:* these pictures are reprints from the cine film of the operation.)

Another incision was made over the base of the left corpus cavernosum and a subcutaneous tunnel was fashioned between the 2 incisions. The divided saphenous vein was passed through the tunnel. An elliptical incision was then made over the left corpus cavernosum. Thick, oily, dark blood rolled out. This was accompanied by an immediate and dramatic " deflation " of the phallus, with the blood becoming brighter and of more normal consistency. The anastomosis between the corpus cavernosum and saphenous vein was then carried out using a continuous suture technique with 00000 Deknatel vascular suture material. Heparin solution was injected in the corpus before the completion of the anastomosis.

After the anastomosis was completed, pressure on the phallus caused the saphenous vein to swell, indicating that drainage was efficient (Fig. 2). The wounds were closed and an Esmarch tourniquet was applied for the purpose of providing smooth continuous pressure to the penis. This was later replaced by a sphygmomanometer with a pediatric cuff, pressure being maintained at 60-80 mm. Hg by the patient himself. Twelve hours later the penis was somewhat œdematous, though flaccid, but tended to become erect slowly with the external pressure removed. Heparin therapy was started on the 2nd post-operative day as well as oral œstrogens. On the 3rd post-operative day the œdema had subsided markedly, and little tendency to erection noted. On the 4th day the penis remained completely flaccid without pressure for several hours.

The patient was discharged on the 6th post-operative day on short-term œstrogen therapy (Fig. 3).

Erections were partially resumed 6 weeks later. Eight weeks post-operatively, full erections were obtained for the first time and the patient was enjoying normal intercourse 3 times a week.

DISCUSSION

In selecting the appropriate mode of treatment for a condition like priapism, it is necessary to look into the pathophysiology involved, and although the physiology of erection has been extensively described by Conti (1952), the exact mechanism that brings about idiopathic priapism remains unknown.

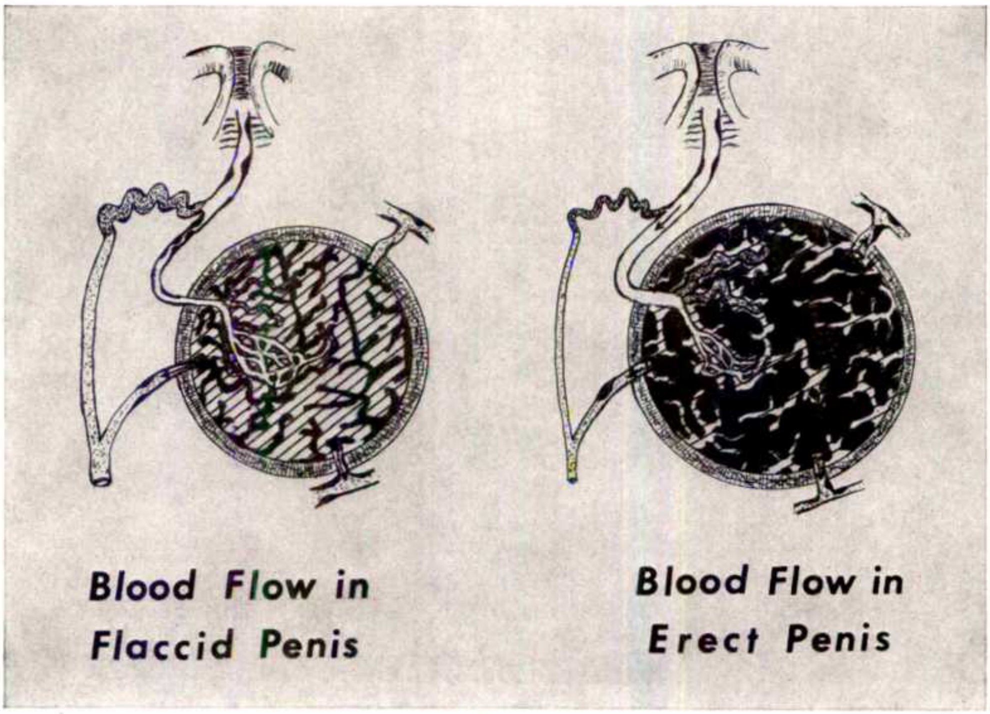


FIG. 4

In the flaccid state the " polsters " in arteries distal to A-V anastomosis are swollen and decrease arterial calibre, thus shunting blood away from corpora, whereas, polsters in drainage veins are relaxed. In erection, polsters in shunt and drainage veins are closed and those in arteries are wide open, thus causing cavernous sinuses to become engorged with blood.

In 1952 Conti studied 20 normal phalli from individuals whose ages varied from birth to 77, and confirmed histologically the presence of " polsters " within the smaller arteries and veins of the penis. These polsters were first described by Stieve in 1930 as muscular pillars or cushions lying longitudinally within the vessel walls. In the flaccid state the polsters in the arteries distal to the A-V anastomoses decrease the arterial calibre and shunt the blood away from the corpora. The polsters in the drainage veins, on the contrary, are relaxed so that drainage is complete.

In erection, the cushions in the shunt as well as those in the drainage veins are closed, whereas the arteries are wide open; the cavernous sinuses become engorged and erection results (Fig. 4).

Vasodilatation is initiated by the lumbar sympathetic nerves which act by inhibiting vasoconstriction and by way of the parasympathetic nerves S_2-S_4 which cause vasodilatation of the arterioles. This was demonstrated by direct stimulation in dogs (Henderson and Roepke, 1933). Sections of the corpora of priapism victims show œdema and fibrosis of the normally delicate fronds making up the corpora cavernosa, thus preventing blood from entering the lacunæ of the corpora and resulting in impotence.

TABLE I

Pathophysiology of Priapism

Neurogenic	psychic stimuli, local sensation	1. Previous episodes; prolonged sexual excitement
	↓ lumbar-sacral centres	
	↓ arteriolar vasodilation	
	↓ ERECTION	
Mechanical	stasis	2. C. cavernosa only
	↓	3. Dark thick blood
	increased CO_2 tension	4. Refilling after aspiration
	↓ increased blood viscosity; œdema	5. Limited subsidence
	↓ greater insufficiency of venous drainage	
	↓ PRIAPISM	
	↓ arteriolar occlusion, fibrosis	6. Eventual non-refilling
	↓ SUBSIDENCE	7. Impotency

(From F. Hinman Jr. (1960). *J. Urol.* **83**, 420.)

The pathophysiology of priapism is summarised in Table I.

It seems that the stasis and increased CO_2 tension initiate a vicious circle that causes more damage to the delicate cavernous endothelium which ultimately leads to a useless fibrotic organ. Useful therapy should therefore be directed at breaking the vicious circle at some vulnerable point.

It appears that the caverno-saphenous by-pass attains this objective by diverting blood from the engorged corpora via the transposed saphenous vein to the general circulation, thus by-passing the œdematous tissues at the base of the corpora.

It seems obvious from the foregoing that in order for therapy to be successful the shunt must function before any irreversible damage has occurred to the corpora, and although thrombosis is reported to occur within the shunt itself within variable periods of the time varying between a few days to a few months, it seems that by that time it has already served its purpose and normal erections can be resumed.

The rapidity with which the priapism subsided in our case, after the corpus cavernosum was incised, indicates the presence of communicating venous channels between both corpora.

However, these may become blocked and a unilateral shunt may only cause a partial subsidence. In such cases it is advisable to perform the operation on both sides, either at the same sitting or a short while later, depending on the response obtained by the first shunt.

Unilateral ligation of the internal pudendal artery causes a decrease in vascularity of the phallus but is fraught with the danger of post-operative impotence. This concern was voiced by Farrer and Goodwin (1961) and shared by Grayhack and his associates, in spite of the preservation of sexual function that followed the experience of Burt, Schirmer and Scott (1960).

SUMMARY

A case of idiopathic priapism in a 27-year-old white male is reported. This was rapidly treated by caverno-saphenous shunt as soon as it was noticed that the response to more conservative measures was poor. The results were satisfactory.

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A FURTHER CASE OF URETERIC DIVERTICULUM—CONGENITAL OR ACQUIRED?

By K. H. CRUMPLIN,[1] F.R.C.S., and S. M. JONES, M.B., Ch.B.

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THIS interesting abnormality is a rare, ill-classified malformation which has found its way into the literature, mainly in urological journals, since 1911. The true incidence is difficult to assess, but from 18,400 consecutive urological admissions at the Royal Victoria Hospital, Montreal, the incidence was quoted as 0·034 per cent of these selected patients (Smith and Orkin, 1945). There has been no series reporting this abnormality on autopsy material, which is interesting in so far as the malformation does not seem to occur as a symptomless incidental finding. Lindemann reported producing ureteric diverticula experimentally in young rabbits by ligating their ureters (Lindemann, 1895). Lotsi was credited with presenting the first case of ureteric diverticulum in 1911. This was an hydronephrosis in fact, and Culp (1947) cites Stevens (1926) with the first case of true congenital diverticulum reported. Until 1947, 52 cases of ureteric diverticulum were documented. Culp reviewed the literature up to that date and presented a case of his own. His findings are pertinent and will be discussed later, but he decided that only 10 of the 52 cases were in fact true congenital ureteric diverticula.

Since 1947 there appear to have been another 21 case reports of ureteric diverticula (Culp, 1947; Mayers, 1949; Harlin and Atkinson, 1950; Barbey, 1952; McGraw and Culp, 1952; Bowie *et al.*, 1954; El Etribi, 1957; Holly and Sumcad, 1957; Dolan and Kirkpatrick, 1960; Mims, 1960; Norman and Dubowy, 1960; Rank *et al.*, 1960; Baines, 1962; Williams and Goodwin, 1965; Rubenstein *et al.*, 1968; Dastur *et al.*, 1969), 12 of these cases being multiple ureteric diverticula, a separate entity.

It is intended to present a further case of true ureteric diverticulum and discuss further its ætiology.

Case History.—C. G., a 63-year-old Irishman, was admitted to hospital on 20th April 1970 with a history of a cough, hæmaturia and lower abdominal pain maximal on the right side. Sometime before the Second World War he had had pulmonary tuberculosis and had received no chemotherapy.

Physical Examination revealed a thin man with a blood pressure of 240/110 mm. Hg. On general examination nothing abnormal was found.

Laboratory Data.—Examination of the blood revealed Hb. 14·5 g., W.B.C. 6,600 c.mm., E.S.R. 3 mm./hr., and blood urea 26 mg. per cent.

Urine Analysis.—Urine analysis revealed no white or red blood cells present in the centrifuged deposit. The urine was sterile. Early morning urine specimens were sent for Ziehl-Neelsen staining and culture for tubercle bacilli. These were all negative.

Intravenous Pyelography was performed and showed a normal left kidney and ureter. There was poor excretion on the right side, and the right kidney was small.

Cystoscopy showed no evidence of active or healed vesical tuberculosis, so *Retrograde Pyelography* was carried out. This showed a large diverticulum of the right ureter at the level of the brim of the pelvis.

Operation.—As there was no evidence of active urinary tuberculosis it was decided to excise the diverticulum without antituberculous drug cover. On 8th May 1969 the right ureter and diverticulum were exposed through an oblique muscle-cutting incision and the sac was excised and an end-to-end anastomosis of the ureter, with splint drainage, was performed.

The patient made an uneventful recovery and was discharged from hospital on 18th May 1969. Follow-up excretory pyelography demonstrated faint visualisation of the right kidney and ureter with no obvious hold-up or dilatation.

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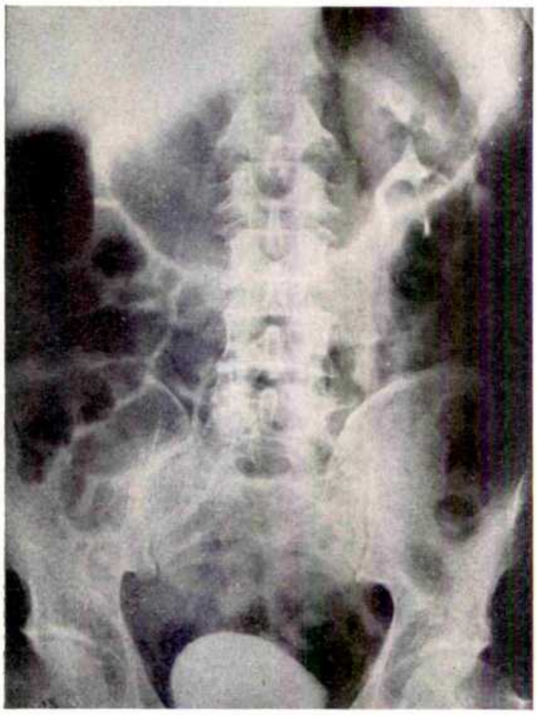

FIG. 1

1. Intravenous pyelogram.

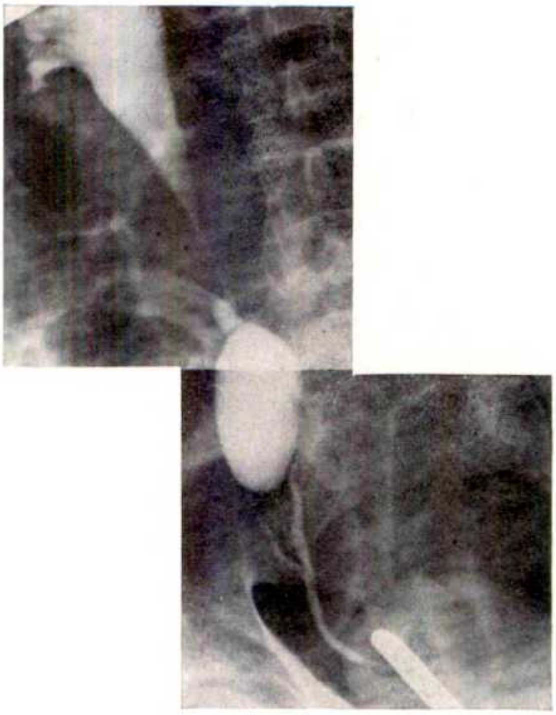

FIG. 2

2. Retrograde pyelogram.

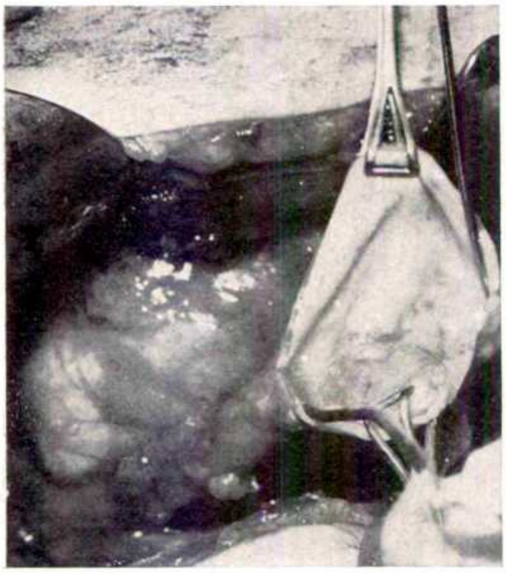

FIG. 3

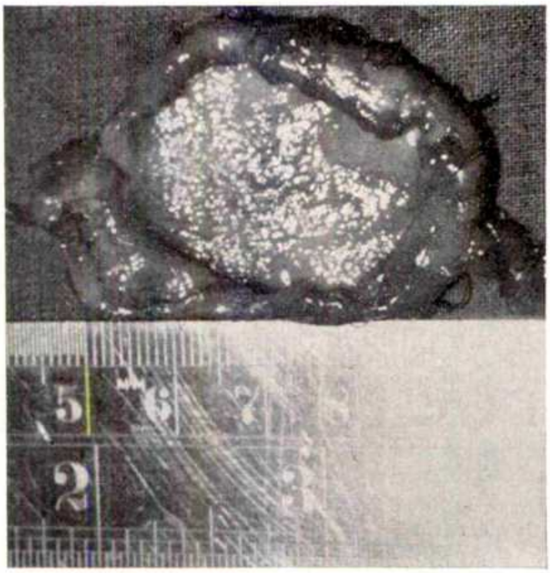

FIG. 4

Fig. 3.—Demonstrating probes inserted into the proximal and distal ends of the ureter entering the sac.

Fig. 4.—Diverticulum laid open.

Pathology.—The sac was an ovoid structure with a large stoma entering into the lateral aspect of the right ureter. There was no stricture of the ureter beyond the sac. The diverticulum measured 4 cm. in length by 3 cm. in breadth. There was some fibrous thickening of the wall, but the normal muscular coats of the ureter were represented. The epithelium was present, but was largely replaced by a thin layer of granulation tissue.

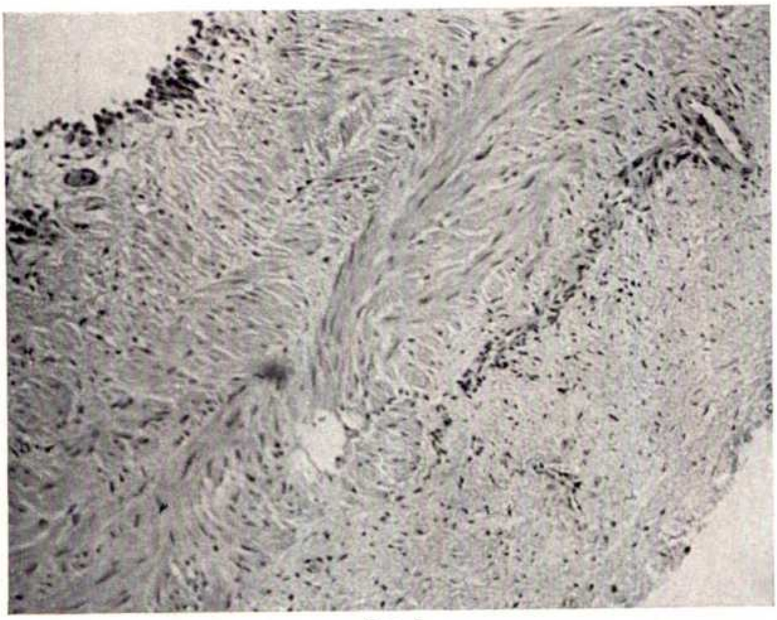

FIG. 5

Histological preparation showing that all layers of the ureter were present.

DISCUSSION AND ÆTIOLOGY

In 1947, Culp reviewed 52 cases of supposed ureteric diverticula. On good evidence, he selected only 10 cases of true congenital diverticulum and 5 acquired cases. Figure 6 is the diagram of the cases he eliminated, also a blind-ending bifid ureter and a true congenital diverticulum. His criteria for distinguishing a true congenital diverticulum were as follows:

1. A round or ovoid extra ureteral sac. This, with his proviso of the diameter of the sac being greater than its length, served to distinguish the lesion from a blind-ending bifid ureter.
2. All coats of the ureter should be represented. This is a necessary part of the definition, but surely, as so many of the cases present clinically with infection as a complication or even occasionally calculi, some of the mucosa may well be destroyed. In the case of a large sac, the muscle layers may be extremely attenuated.
3. The communication of the sac with the ureter should have a distinct stoma. The size of this stoma seems to vary a good deal in the cases presented.

A true congenital diverticulum is clearly an extremely rare abnormality and it has been presumed that all 10 cases that Culp described existed as congenital lesions. It must be stated, however, that little is known of their pathogenesis. Most cases present in adults and it has never been recorded as a symptomless, incidental finding, as have been many other ureteral abnormalities. Culp's own original case, quoted in 1947, describes a man who received shrapnel injuries of the abdomen, for which the patient underwent small bowel resections. Nothing abnormal was found in the patient's left renal area at operation; however, a few weeks later further laparotomy for a large intra-abdominal mass revealed a ureteric diverticulum with a capacity of 1,500 cc. Clearly this had developed since the first laparotomy. Could this not have been due to the injuries received? It is surely impossible to say.

In the case presented here, the criteria laid down by Culp for a true congenital diverticulum are fulfilled, but the patient may well have had urinary tuberculosis in the past, and although there was no stricture distal to the sac, it is again difficult to rule out the fact that the abnormality may have arisen as a result of urinary tuberculosis.

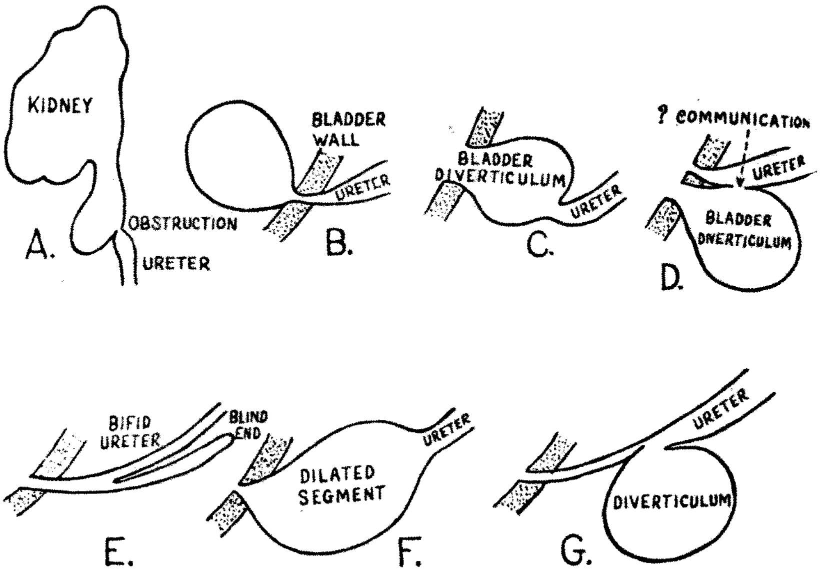

FIG. 6

Figure showing cases that Culp excluded from his series of ureteric diverticulum, a blind-ending bifid ureter and a true congenital diverticulum of ureter. (Reprinted from *Journal of Urology*, 1947—Culp, O. S.)

The histology of the ureteric diverticulum is identical to that of a blind-ending bifid ureter. Both of these lesions may occur anywhere along the ureter—more commonly at the upper or lower end. If one is to suggest a different ætiology from premature cleavage of the ureteric bud (as in the case of a blind-ending bifid ureter), then it would presumably have to be a local neurological or muscular defect in the ureteric wall. It may well be the case that the true congenital ureteric diverticulum is a variant of the blind supernumerary ureter which assumes a different shape due to disease or pressure changes along the ureter.

Twelve cases of multiple ureteric diverticula have been noted in the literature (Holly and Sumcad, 1957; Dolan and Kirkpatrick, 1960; Mims, 1960; Norman and Dubowy, 1960; Rank *et al.*, 1960; Baines, 1962; Williams and Goodwin, 1965). This represents a recently described abnormality. These cases are usually associated with urinary tract infection and it has been interesting to note that 15 per cent of patients with urinary tract infection have microscopic evidence of cystic changes in the ureter (Bothe and Cristol, 1942). On one occasion nephroureterectomy was performed (Williams and Goodwin, 1965), but few cases have received operative intervention. Failure of the collecting tubules to be absorbed into the major calyces has been suggested as an ætiological factor in the formation of multiple diverticula at the upper end of the ureter (Williams and Goodwin, 1965).

SUMMARY

A further case of true ureteric diverticulum is presented. As in some other cases, its origin is presumed congenital but the possibility of an acquired ætiology cannot be discounted. Whether or not the lesion starts as a local defect of the ureteric wall, or as a blind-ending bifid ureter, remains unproven.

We are indebted to Mr E. J. C. Wynne for his permission to present his patient in this article. We also wish to thank Mr P. E. Huddy and Mr P. H. Powley for their helpful advice and criticism, and to Miss L. Lemon, and to the Photographic Department, for their invaluable help.

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ARTERIAL CHANGES ASSOCIATED WITH HYDRONEPHROSIS IN INFANTS AND CHILDREN

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IN the course of a study into the effects of back-pressure on the developing human kidney it was noticed that many kidneys showed damage to the larger arteries which was remarkably similar to that described in experimental hydronephrosis in animals (Sheehan and Davis, 1959). These changes have not previously been described in children's kidneys and in this age-group atherosclerosis plays little or no role in their pathogenesis.

Material and Methods.—During the period 1951 to 1967 hydronephrosis was recorded at post-mortem or at nephrectomy in 125 patients. Sixty-three kidneys from 43 children were preserved in formol-saline and were available for study. The ages of the patients ranged from birth to 14 years with 30 (47 kidneys) less than 12 months. Organic obstruction of the ureters or urethra was present in the case of 40 kidneys, whilst in 23 no anatomical obstruction could be demonstrated. Among the latter group vesico-ureteric reflux was demonstrated during life in 6 kidneys and it was suspected after death in a further 15 because the ureters and their vesical openings were dilated. Children with absent abdominal muscles were not included in the study.

TABLE I

Classification of Kidneys

Group	Criteria	Numbers
I	Pelvic dilatation alone	14
II	Dilatation of minor calyces and blunting of papillæ	10
III	Flattening or concavity of papillæ	35
IV	Hydronephrosis at P.M., not evident after formol-saline fixation	4
		63
Control	(i) Normal kidney from patients with contralateral hydronephrosis	7
	(ii) Normal kidneys	17
		24

The kidneys were placed in four groups according to the severity of hydronephrosis (Table I). Group I consisted of 14 kidneys in which there was dilatation of the renal pelvis but not of the minor calyces. In Group II there were 10 kidneys in which there was dilatation of the minor calyces with blunting but not complete flattening of the renal papillæ. Group III contained 35 kidneys whose papillæ had lost their normal convexity so that they formed concave ends to the dilated minor calyces. Finally Group IV contained 4 kidneys in which dilatation of the renal pelvis had led to a diagnosis of mild hydronephrosis at post-mortem but which, after formalin fixation, appeared normal to the naked eye.

Controls were obtained from two sources. In 7 patients there was either a whole kidney or half a duplex kidney which was not obstructed and which was available for study. In addition, renal tissue was examined from 17 children with normal kidneys whose age (or body weight of neonates), sex and year of death matched those of the 17 children in the study in whom an organic obstruction of the lower urinary tract was found at post-mortem.

The neonatal kidneys were bisected in the coronal plane, slices from the entire cut surfaces were then embedded in paraffin wax and 5-μ sections were cut. From the larger kidneys 2 or 3 blocks of tissue were taken from different areas so that each showed a complete cross-section of a renal lobe from the capsule to its papillary surface. These blocks included interlobar arteries in all cases and a segmental artery in most. No attempt was made to include the main renal artery. Sections 5-μ thick were stained with Verhoff's stain for elastin, hæmatoxylin and eosin, periodic-acid Schiff, Azan's trichrome and Perl's stain for iron. In combination these demonstrated details of the arterial elastic tissue and made it possible to say whether intimal proliferation or abnormalities of the internal elastic lamina (I.E.L.) were related to branching of the arteries (Fig. 1).

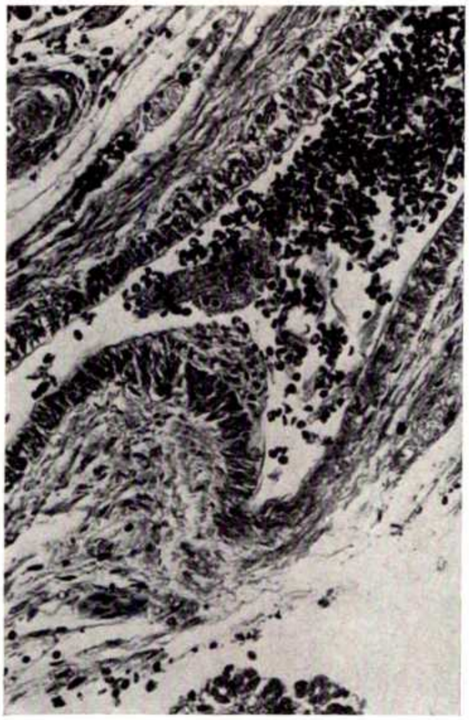

FIG. 1

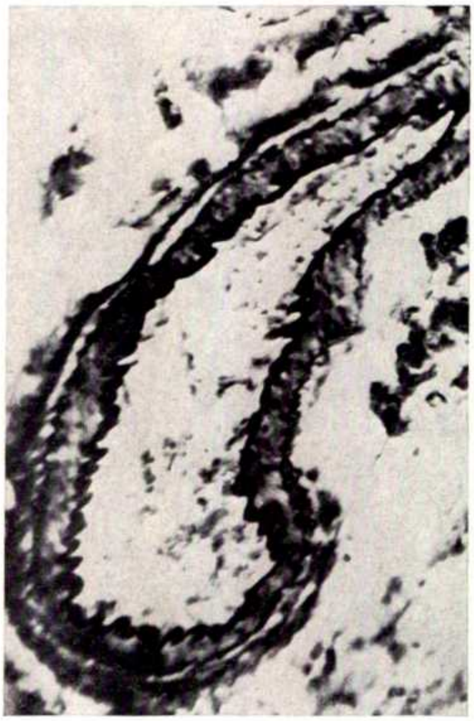

FIG. 2

Fig. 1.—Intimal cushion at the bifurcation of an interlobar artery in a control kidney. Azan. × 192.

Fig. 2.—Normal interlobar artery showing uninterrupted I.E.L. and unicellular intima. Verhoff. × 150.

Histological abnormalities in each kidney were graded 1, 2 or 3 according to their prevalence and severity. The arteries were examined with special care for the presence of thrombosis, intimal proliferation, reduplication or splitting of the I.E.L. and hypertrophy of the media, although these were disregarded if they appeared to be related to the origin of an arterial branch.

Findings.—In a normal muscular artery the I.E.L. forms an unbroken elastic membrane beneath the intima which is a unicellular layer (Fig. 2). Breaks in the I.E.L. of the arteries in this study were occasionally single but usually multiple (Fig. 3). However, even multiple breaks were confined to a small segment of the lamina. With a single break there was usually no evidence of any local tissue reaction (Fig. 4) but multiple breaks were associated with changes in the adjacent I.E.L. and intima. Repair of the I.E.L. appeared either as reduplication in which there was a single complete layer of elastin internal to the ruptures (Fig. 5) or as splitting in which there were multiple fine layers of elastin (Fig. 6) internal to the breaks. With splitting of the I.E.L., none of the fresh layers of elastin completely bridged the ruptures over which they formed an overlapping network. Reduplication or splitting of the I.E.L. was usually accompanied by thickening of the intima by longitudinal smooth muscle fibres interspersed with elastic fibrils and sometimes also with collagen (Fig. 7). This intimal proliferation extended beyond the area of ruptured I.E.L. so that occasionally it was seen over an apparently intact lamina. Intimal proliferations were usually small and involved only a small segment of the circumference (Fig. 5), but in the most severely affected arteries they caused a marked reduction in the size of the lumen (Fig. 8). The incidence of breaks in the I.E.L., of splitting or reduplication of the I.E.L. and of intimal proliferation in the four groups of kidneys is shown in Figure 9.

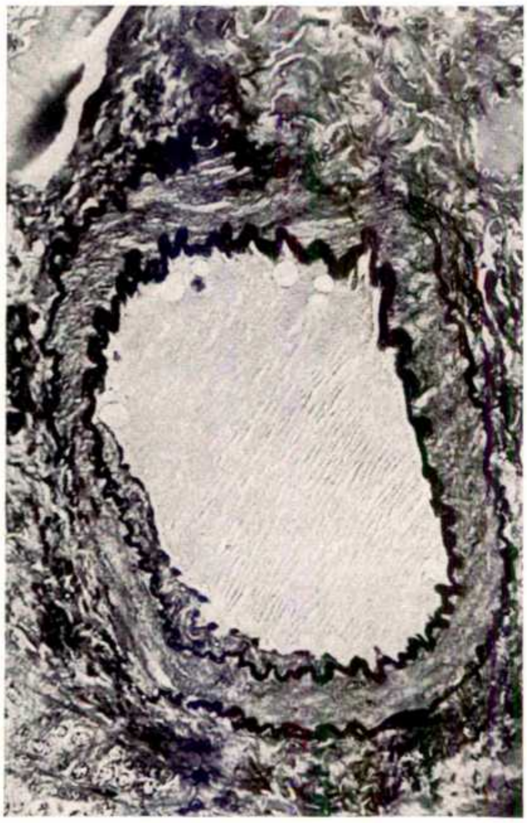
FIG. 3

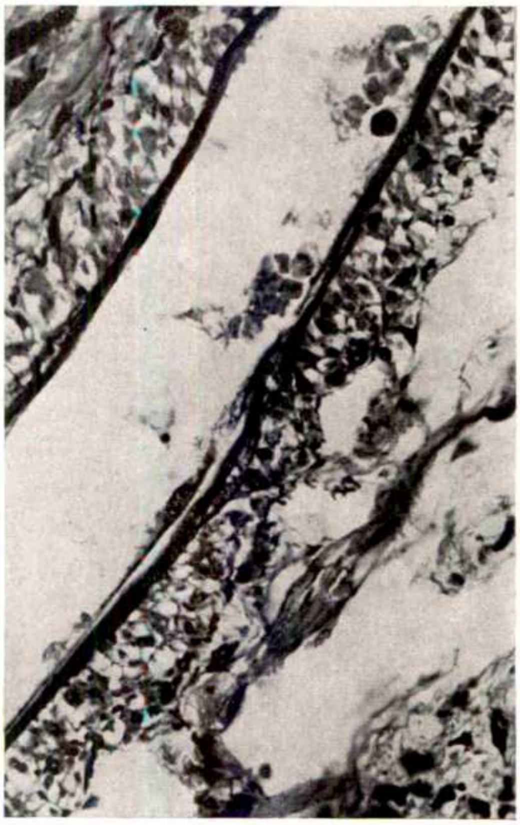
FIG. 4

Fig. 3.—Thinning and fragmentation of the I.E.L. with minor intimal proliferation in an arcuate artery. Boy aged 2 years with staghorn calculus in group III. Verhoff. × 300.

Fig. 4.—Single break in the I.E.L. of an arcuate artery with intimal reaction in a control kidney. Verhoff. × 480.

These changes were present in the segmental, interlobar or arcuate arteries but were rarely seen in the interlobular arteries which are smaller and run peripherally from the cortico-medullary junction. The degree of abnormality and the number of arteries affected in any one kidney were found to be related to the severity of hydronephrotic change in the kidney and probably to the age of the patient. It is probable that local intimal proliferations form the site of atherosclerosis in the older patient (Robertson, 1960*a*) but deposits of lipid were not seen in the arteries in the present series. In patients under 1 year the changes were confined to the intima and I.E.L. without abnormality of the underlying media. However, in kidneys from patients older than 1 year there was occasionally thinning and fibrosis of the media beneath large intimal proliferations but not beneath isolated breaks in the I.E.L. (Fig. 8).

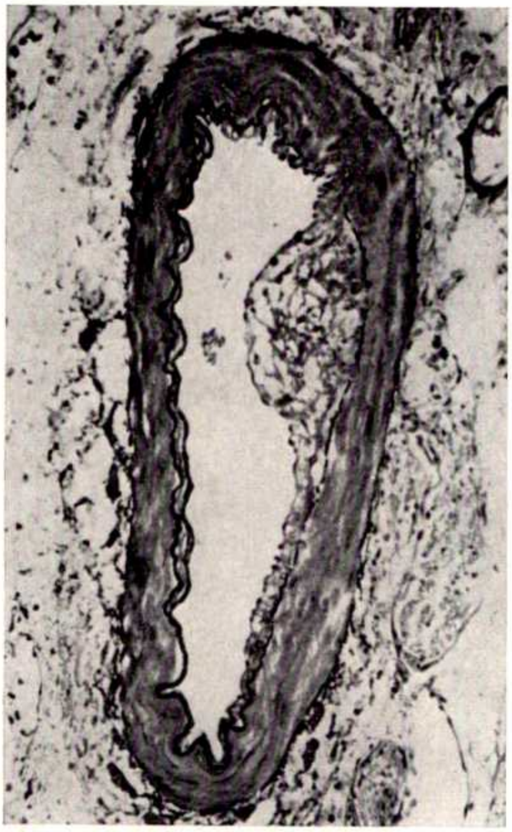

FIG. 5

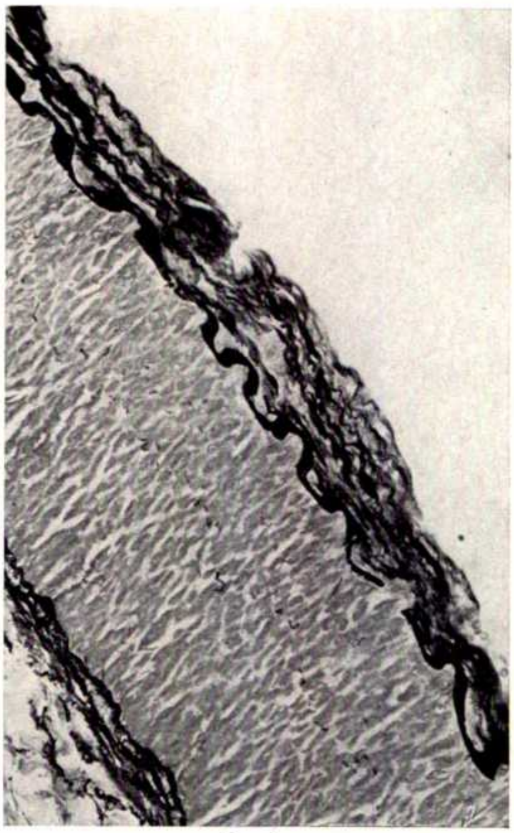

FIG. 6

Fig. 5.—Interlobar artery showing reduplication of the I.E.L. opposite a small intimal elastic cushion. Beneath the cushion the I.E.L. is thin and fragmented. Group III kidney with pelvi-ureteric junction obstruction. Verhoff. × 150.

Fig. 6.—Two small breaks and splitting of the I.E.L. in a segmental artery. Group III kidney with pelvi-ureteric junction obstruction in 11½-year-old boy. Verhoff. × 192.

Definite thickening of the media, either local or generalised, was seen only in the arteries of 1 child who suffered from malignant hypertension. Arterial thromboses were found in nephrostomy scars in three kidneys and were associated with severe acute pyelonephritis in 2 others. It is therefore felt that these lesions did not result from obstruction *per se*.

Abnormalities of the intima or I.E.L. of the larger arteries appeared to be unrelated to the origins of branches in 8 (33 per cent) control kidneys. Similar lesions were found in 9 kidneys (64 per cent) in Group I, 7 kidneys (70 per cent) in Group II, 31 kidneys (89 per cent) in Group III and 3 kidneys (75 per cent) in Group IV. The differences between the control kidneys and those in Groups I and II are not statistically significant[1] ($P > 0\cdot05$) whether the groups are assessed separately or together. There is, however, a highly significant difference between the controls and

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[1] Statistical analysis by χ^2 test using Yates' correction for binomial distribution.

Group III ($P > 0{\cdot}001$) and the differences between Group III and Groups I and II combined is probably also significant ($P < 0{\cdot}05 > 0{\cdot}01$). The results of Group IV cannot be analysed statistically because of the small numbers involved.

With increasing age there was a tendency for the number of kidneys showing intimal or I.E.L. damage in the larger arteries to increase (Fig. 10). Thus, taking the obstructed kidneys as a whole, 78 per cent of those from children aged less than 1 year showed damage compared with 94 per cent of the kidneys from children older than 1 year. While suggestive, these figures are not statistically significant ($P > 0{\cdot}05$). On the other hand, the degree of intimal thickening and consequent reduction of the arterial lumen was much greater in the older children.

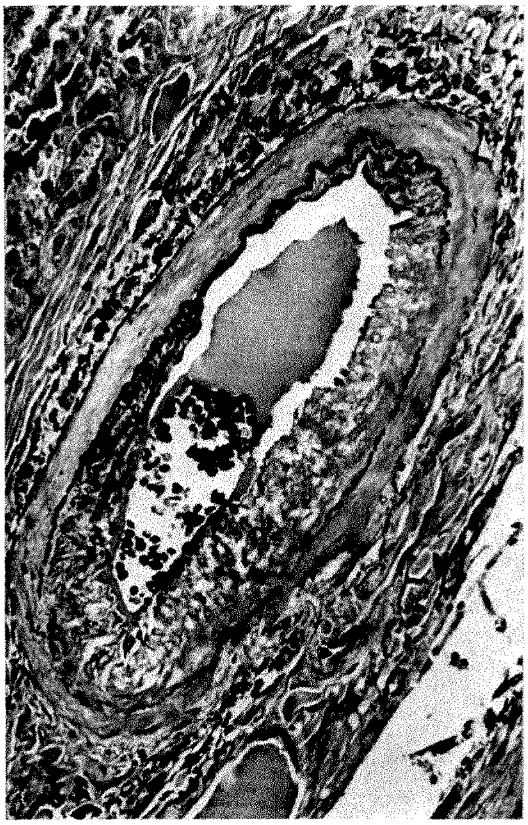

FIG. 7

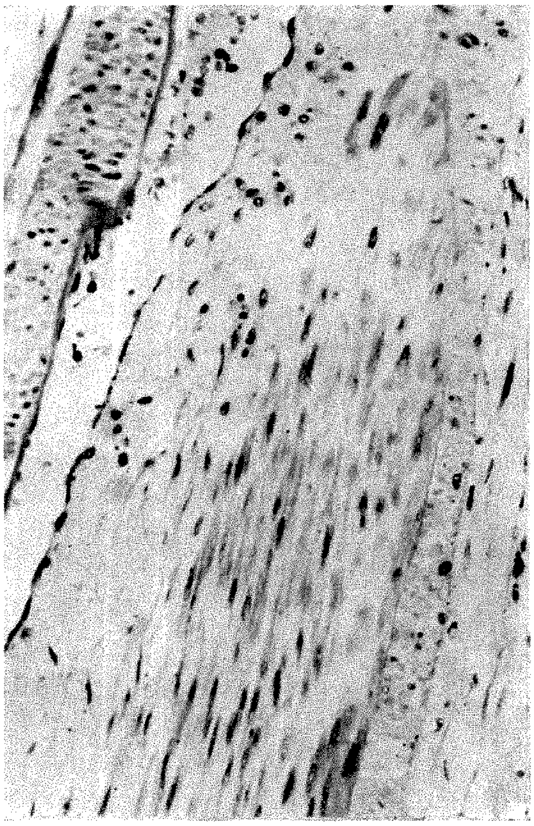

FIG. 8

Fig. 7.—Large intimal proliferation narrowing the lumen of an arcuate artery in the group III kidney of a normotensive 14-year-old boy. The underlying I.E.L. is fragmented and it is split at the edges of the proliferation. The media is thin beneath part of the proliferation. Verhoff. × 192.

Fig. 8.—Intimal proliferation consisting chiefly of longitudinal smooth muscle in an interlobar artery from the same kidney as Fig. 7. There is narrowing of the lumen and thinning of the underlying media. Hæmatoxylin and eosin. × 192.

DISCUSSION

Experimental Work.—Similar arterial changes have been described in experimental hydronephrosis in animals. Sheehan and Davis (1959) found ruptures of the I.E.L. of segmental, interlobar and occasionally arcuate arteries of rabbit kidneys subjected to complete obstruction.

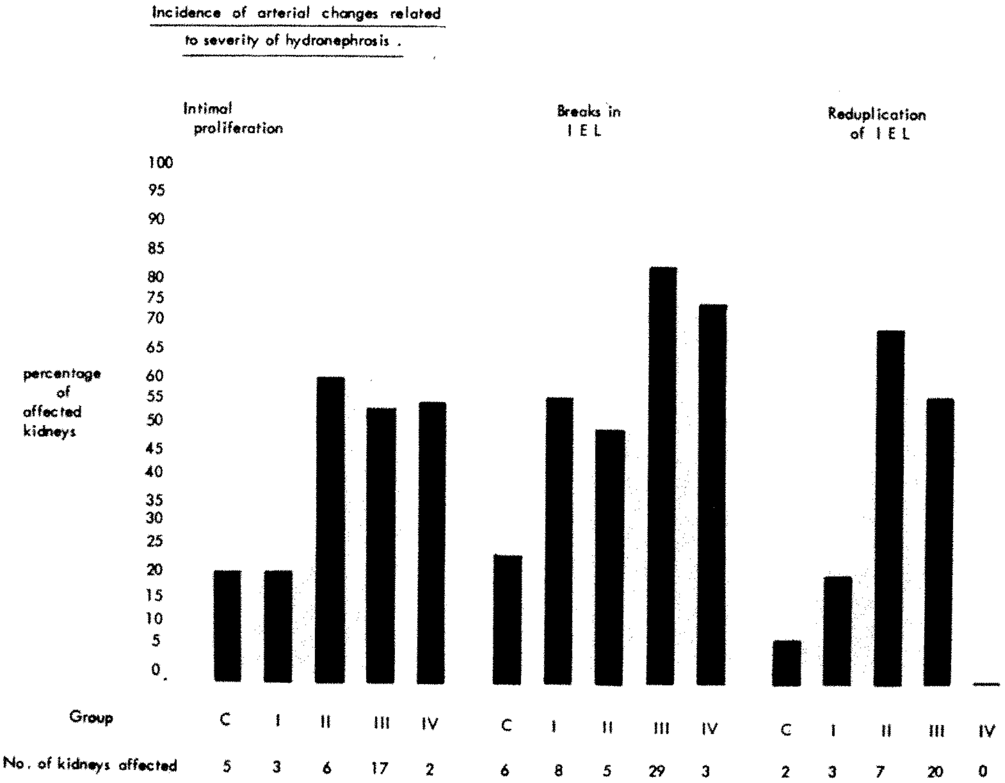

FIG. 9

Incidence of arterial changes related to severity of hydronephrosis.

They appeared within a few days of obstruction, but it was not until 2 weeks or more that fibrous thickening of the intima was demonstrable. At a later stage fine elastic fibrils were laid down in the intima and these thickened and coalesced either to form several thin layers of elastica or to form a single layer of elastica which did not join up with the ends of the original lamina. They concluded that the ruptures resulted from longitudinal stretching of the arteries over the dilated pelvis of the obstructed kidney and that the rate of dilatation influenced the rapidity with which ruptures appeared. They also felt that the process of repair of the ruptures was histologically distinct from " elastic cushions " in which layers of elastin are laid parallel to the I.E.L. often with a deficiency of muscle in the nearby media. These cushions were found equally in obstructed and in control kidneys and they were seen no more frequently after longer periods of complete obstruction.

A different view was taken by Altschul and Fedor (1953), who found transverse and longitudinal tears of the I.E.L. and reduplication of intimal elastin in large arteries after ureteric ligation in rats and rabbits. They also examined human kidneys taken from adults with long-standing hydronephrosis and found elastic reduplication but no tears of the I.E.L. They considered that the elastic reduplication was due to healing of the tears in the I.E.L., but in their human kidneys were unable to distinguish this from the effects of arteriosclerosis. There have been no other reports of arterial changes in human hydronephrotic kidneys.

The main objection to the use of rats and rabbits is that their kidneys have only 1 papilla each. In view of this Matz, Hodson and Craven (1969) used the multipapillary kidney of the pig which is similar in size and anatomy to the human kidney. Two groups of pigs were subjected to unilateral ureteric ligation for periods up to 28 days followed by immediate sacrifice or repair

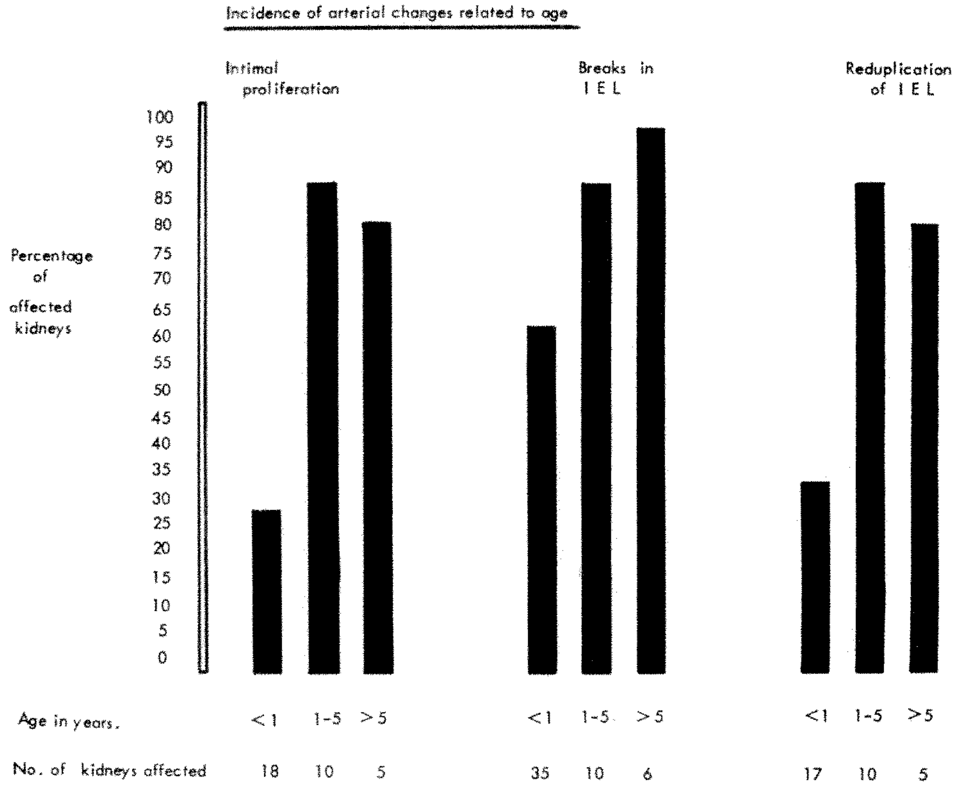

FIG. 10

Relationship of arterial changes to the age of the patient.

of the ureter and sacrifice 6 months later. They found fragmentation or deficiencies of the I.E.L. of the main renal arteries, their proximal extra-renal branches and occasionally their intra-renal branches in every obstructed kidney. In 3 out of 10 animals similar, but much less severe, changes were seen in the corresponding vessels on the unobstructed side. They found that in the obstructed kidneys elastic reduplication, thicker elastic fragments and intimal pads of smooth muscle or connective tissue became more marked as the period between ureteric ligation and death increased. This supports the concept that elastic cushions represent a healing process. These authors found that mechanical stretching could not account for all the observed arterial changes. They adduced evidence that long-continued arterial constriction occurs in the early stages of ureteric ligation, and they suggested that it may contribute to the damage.

Elastic Cushions.—Elastic cushions similar to those observed in the present study have been described in the human fœtus in the coronary arteries (Dock, 1946; Fangman and Hellwig, 1947; Levene, 1956) the popliteal and distal end of the brachial arteries (Robertson, 1960*a*) and the renal arteries (Müller, 1954). They are usually found at the origins of branches and are believed to develop in response to mechanical stress at the points where the arterial wall is relatively immobile. With increasing age they become more numerous and by the second decade they may be found in the femoral and occasionally in the posterior tibial and radial arteries (Robertson, 1960*b*). Their pathological significance lies in the fact that atherosclerosis tends to develop in them during later life in individuals prone to this disease (Duguid, 1926; Robertson, 1960*b*).

Present Investigation.—In the present series an attempt was made to eliminate arterial changes associated with the origins of branches by examining serial sections. It was not possible to form an accurate estimate of the duration of obstruction in any of the kidneys examined and the only means of assessing the severity of obstruction was the crude one of macroscopic appearance. Since there was no evidence that any kidney was totally obstructed it must be assumed that in most cases the rate of development of hydronephrosis had been slow. This may account for the fact that intimal changes were not seen in all of the Group III kidneys. The finding of localised intimal proliferation and elastic reduplication in 20 per cent of the control group and breaks in the I.E.L. in 25 per cent suggests that factors other than back pressure on the kidney are involved in the production of arterial lesions. One such factor could be a prolonged period of arterial constriction as suggested by Matz *et al.* (1969).

In spite of these drawbacks the findings show conclusively that the arterial features described in experimental hydronephrosis in animals are also found in severely hydronephrotic human kidneys in infancy and childhood. The age of our patients and their other clinical and pathological features exclude atherosclerosis as a possible cause of the lesions.

Of the 11 kidneys in Group III in whom no organic obstruction could be found, ureteric reflux was demonstrated radiographically during life in 4 and in a further 4 reflux was suggested by the finding of a widely dilated ureteric orifice and ureter at post-mortem. Arterial changes were found in 7 of these 8 kidneys which in no way differed from the changes in the other members of the group. It is known that severe reflux may produce the radiographic appearance of hydronephrosis in infantile kidneys (Rolleston, Shannon and Utley, 1970) and our findings suggest that the pathological effects are also indistinguishable from those of organic obstruction.

Previous studies have shown that atherosclerosis is likely to develop at the sites of elastic cushions in susceptible patients. The present study draws attention to the fact that once a kidney has been subjected to back pressure for a sufficient length of time to produce cupping of the calyces, its arteries are likely to show abnormal intimal proliferation. Thus, paradoxically, preservation of such a kidney through relief of obstruction may put the patient at risk of developing atherosclerotic renal artery stenosis and hypertension in the future. Although hypertension is uncommon in adult patients presenting with hydronephrosis (Rubtsov, 1967), there are no published figures for the incidence of hypertension developing after the surgical relief of urinary tract obstruction. There is therefore a need for long-term follow up studies so that the true risk to these patients may be assessed.

SUMMARY

Sixty-three hydronephrotic kidneys from children have been studied. Arterial damage in the form of intimal elastic cushions and breaks in the internal elastic lamina was found in the interlobar and arcuate arteries of the majority. It was more common in more severely hydronephrotic kidneys and with increasing age of the patient the elastic cushions appeared larger. The damage is thought to result from increased pressure in the lower urinary tract due to obstruction or to severe vesico-ureteric reflux. It is suggested that the arterial damage may predispose the patient to atherosclerotic reno-prival hypertension.

We are deeply grateful to Mrs F. Byron, without whose patience and expert technical assistance this study would not have been possible. M. H. W. was in receipt of a Nuffield Trust research fellowship which is gratefully acknowledged.

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MULTICENTRE SURVEY OF URINARY TRACT INFECTIONS IN GENERAL PRACTICE

Clinical Trial of Single Dose Treatment with Sulfametopyrazine (Kelfizine-W)

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THE management of urinary tract infections in general practice is beset with problems. It may be difficult to confirm the presence of a true infection; subsequent chemotherapy is often incomplete by default and there is in addition the problem of the chronic or recurrent case and when to refer such patients for hospital investigation.

It would seem that up to half the women presenting to their family doctors with symptoms referable to the urinary tract have sterile bladder urine (Mond *et al.*, 1965; Gruneberg and Brumfitt, 1967; Cudmore, 1970) and in this group it is obviously undesirable to continue prolonged courses of expensive antibacterial agents. At the same time patients commonly discontinue the full course of tablets prescribed as soon as symptomatic relief is obtained (Sprunt, 1970)—as examination of the average family bathroom drug cabinet may confirm. Where a true urinary infection exists this may result in suppression rather than elimination of the causal organism which re-appears in clinical significance some weeks later at which time it may have acquired resistance to the agent first used.

This clinical survey of patients seen in 6 urban practices was carried out to assess the incidence of true urinary tract infections, to ascertain the sulphonamide sensitivity of such infections and to carry out a controlled trial of a single dose treatment, namely, sulfametopyrazine (Kelfizine-W), an ultra long-acting sulphonamide new to the United Kingdom.

Pharmacokinetics.—Sulfametopyrazine has an uncommonly low-protein binding propensity for a long-acting sulphonamide. A figure of around 60 per cent at therapeutic blood levels is usually quoted (Wiegand *et al.*, 1964). The dissociation constant of its complex with the plasma albumin is high, so that the relative proportion of free sulphonamide in the plasma is also high (Berlin, 1964). The pKa of sulfametopyrazine is 6·3, which means that at this pH it will be 50 per cent un-ionised. As the pH falls, the proportion of un-ionised sulphonamide increases and it is this fraction which is available for reabsorption in the proximal renal tubules. Over the usual pH range of urine, therefore, there is a constant supply of un-ionised sulphonamide available for reabsorption and it is this which is mainly responsible for the long biological half-life of 65 hours (Berlin, Wiegand *et al.*). Conversely, if the pH be raised, as by giving alkali, the proportion of un-ionised sulphonamide will fall, tubular reabsorption will be diminished and excretion thereby increased.

A single dose of 2 grammes of sulfametopyrazine produces blood levels of over 100 mg./ml. which decline to about 30 mcg./ml. by the 7th day (Salvi *et al.*, 1963). Once a week administration of 2 grammes results in the maintenance of bacteriostatic blood levels without drug accumulation in the presence of normal renal function.

For the above reasons it was considered that sulfametopyrazine would be an effective and convenient once-a-week treatment in primary urinary tract infection as encountered in general medical practice.

Patients and Methods.—Patients visiting their family doctors with symptoms referable to the urinary tract were admitted to the trial. None had received recent treatment. A mid-stream urine was obtained and treatment given either with sulfametopyrazine (Kelfizine-W) 2 g. in a single tablet, or with ampicillin 500 mg. 8 hourly for 7 days—decided by random selection. Further urine specimens were obtained at 12 and 19 days and at 6 weeks. Assessment of clinical response to treatment was made and a pro-forma completed. Cross-over treatment from one drug to the other was made during the period of the trial in the event of failure to respond clinically, or if drug hypersensitivity reactions occurred. Patients who failed to respond to treatment, or remained symptomatic were referred to hospital for urological investigation.

Examination of Urine.—Mid-stream specimens of urine were collected by the clean catch technique and were sent to the laboratory in 28 ml. universal bottles containing 0·5 g. of powdered boric acid (Porter and Brodie, 1969). White cells were counted per high-power field. The specimens were cultured on blood agar and MacConky agar. Bacterial counts were carried out by a standard loop technique. A true urinary infection was defined as that showing a count of more than 100,000 organisms per ml. of urine. As the living cell deposit was perfectly preserved by this method of collection the leucocyte count was significant and in almost all infections was greater than 20 per high-power field.

Antibiotic Sensitivities.—These were carried out on Harper and Causton's Medium with discs containing 25 μg. of ampicillin on 200 μg. of sulphatriad.

Results.—Three patients defaulted during follow-up and were lost to the trial. One hundred and thirty-one were included in the survey. All received treatment and completed the follow-up regime (125 females, 6 males). Sixty-six patients (2 males) showed a significant bacteriuria (50 per cent). Table I shows the bacteriology of the 66 infections. It will be seen that 47 of the 52 infections with *Escherichia coli* were sulphonamide sensitive (90 per cent), also all the 5 infections due to *Staph. albus* and 7 out of 9 infections due to *Proteus* strains—an overall sulphonamide *in vitro* sensitivity rate of 89 per cent. In 2 patients with no significant bacteriuria, monilia (*Candida albicans*) was cultured from the urine.

TABLE I

Bacteriology of 66 Infections

Organism	Sulphonamide Sensitive	Sulphonamide Resistant	Sulpha and Ampicillin Resistant	Total
Esch. coli	47	4	1	52
Proteus Spp.	7	2	...	9
Staph. albus	5	...	...	5
Total	...	...	...	66

With regard to the therapeutic response (Table II) there was no significant difference between ampicillin and Kelfizine treatment patients. In the *Escherichia coli* infections 22 of 26 initially treated with Kelfizine were cleared, compared with 21 of 25 in the ampicillin group. Cross-over treatment occurred in 7 patients. In 5 patients a change from ampicillin to Kelfizine was effected because of failure to respond to treatment (2 patients), and side-effects (3 patients). All 5 infections were initially sensitive *in vitro* to sulphonamide and cure resulted. Two patients were crossed over from Kelfizine to ampicillin because of failure to respond clinically (1 initially sulphonamide resistant); both cases were cured. One patient initially treated with ampicillin was found to have *Escherichia coli* resistant to both ampicillin and Kelfizine and was subsequently treated with nalidixic acid, with cure.

In 9 *Proteus* spp. infections (7 sulphonamide sensitive) cure was effected in 2 cases treated by ampicillin, but only 4 of 7 treated by Kelfizine. Of the 3 failures with Kelfizine, however, 2 were in male patients, one of these had a prostatitis with outflow obstruction, and the other declined investigation on leaving the district, but a vesical neoplasm was suspected on clinical grounds.

TABLE II

Therapeutic Response

Drug	*E. coli*		*B. proteus*		*Staph. albus*	
	Treated	Cured	Treated	Cured	Treated	Cured
Sulfametopyrazine	26	22	7	4	3	3
Ampicillin	5	21	2	2	2	2
Cross over Ampicillin→ Sulfametopyrazine	5	5	...	...	...	...
Cross over Sulfametopyrazine Ampicillin	2	2	...	...	...	...

Staph. albus infections: all 5 showed a heavy bacteriuria with a very high leucocyte count and must be considered true urinary tract infections; all were sulphonamide sensitive and responded immediately to treatment.

Side-effects.—Of the 131 patients treated, 58 received ampicillin and 73 received Kelfizine. Seven patients received both ampicillin and Kelfizine. In those patients receiving Kelfizine one developed an urticarial rash (1 in 80 treatments). This was not severe and responded to increased fluid intake and alkalis in 48 hours. Of the patients receiving ampicillin, 4 exhibited side-effects attributable to the drug; 3 showed an urticarial rash (severe in 1 case) and 1 patient a gastro-intestinal upset (4 in 65 treatments).

Referral to Hospital.—Three female patients were investigated in the Urological Department. In 2 no anatomical or functional abnormality in the urinary tract was found and at the time of investigation the urine was sterile. In the third a post-menopausal stricture of the urethra was found and treated by dilatation and hormone therapy. Of the 2 male patients with unresolved infections with *Proteus* spp. one declined investigation and the other has left the district.

DISCUSSION

The relatively low incidence of true urinary tract infection in those patients presenting to their family doctors with symptoms referable to the urinary tract has again been confirmed together with a high (89 per cent) *in vitro* sulphonamide sensitivity of the organisms found. Sulphonamide sensitivity of *E. coli* strains shows a geographical variation in urban populations of the United Kingdom. That of the south-west corresponds very closely with that found in London (Williams and Leigh, 1966) and is higher than that found in the Midlands (Williams and Smith, 1970).

With regard to those female patients with sterile bladder urine, it is likely that the symptoms are due to lower genital tract infections such as those due to *Trichomonas vaginalis* or *Candida* *albicans*, and such gynæcological abnormalities as cervicitis or prolapse or to the urethral syndrome. The last named embraces a wide spectrum of ætiological causes. There may be a distal urethral infection with introital organisms or a purely mechanical or chemical inflammatory œdema of the urethra following coitus. In the post-menopausal group chronic inflammatory change and urethral stenosis results from œstrogen withdrawal atrophy of the urethral mucosa.

In a survey such as we have undertaken it might have been more valuable to have combined culture of the mid-stream urine specimens with that of first stream urine specimens, urethral and introital swabs, but the practical difficulties in general practice precluded this. Culture of urethral swabs in patients referred to hospital with urinary tract symptoms has been unrewarding in our hands to date. There is little doubt, however, that introital enterobacteria show the same serotype as the patients' own rectal organisms and, as demonstrated recently by O'Grady *et al.* (1970), the same serotype as urethral enterobacteria when present. Colonisation of the introitus from the rectum and the urethra from the introitus is a matter of diminishing incidence.

With regard to the therapeutic response to treatment in this series of patients it would appear that sulfametopyrazine was equally effective as ampicillin and with fewer side-effects. It is not claimed that this sulphonamide gives any better results than those of the short-acting variety such as sulphadimidine in which a 90 per cent cure rate has been achieved (Mond *et al.*, 1965), but treatment with an ultra long-acting sulphonamide such as sulfametopyrazine has obvious practical advantages with regard to ease of administration and assurance that the full therapeutic course has been received. The theoretical drawback to this form of therapy is that should a sensitivity reaction occur it will be more prolonged and severe. In this study only 1 patient exhibited side-effects and this was an urticarial rash of moderate severity only which appeared to last no longer than that occurring with the short-acting sulphonamides, and responded to high fluid intake and alkalis in the usual manner. This might be expected by a study of the pharmacokinetics (see above).

The results in this study would suggest that all patients presenting to their doctors with symptoms of urinary tract infection could be conveniently and expeditiously treated by a single dose (2 g.) of an ultra long-acting sulphonamide provided that a urine specimen has been taken for culture either by the dip. inoculum, dip slide or the boric acid techniques. This single treatment would appear to be effective in 90 per cent of cases and would need revision only if there was failure to respond clinically by which time the urine culture results would be available.

The decision to refer such patients to hospital for investigation may be a difficult one and influenced by the fact that those who are most symptomatic often show no infection of the urine. Certainly all children should be investigated after their first confirmed infection as a high proportion show urinary tract pathology (Starer, 1970). In adult women it would probably be impossible to investigate everyone at such a stage, but it is obviously desirable to do so if there is any recurrence of a confirmed urinary tract infection. The indication, on medical grounds, for investigation of those patients with recurrent urinary tract symptoms and non-significant bacteriuria is obviously not so strong, but there is surely a need in these cases for immediate referral to a Urology Out-patient Department *whilst symptomatic* for pelvic examination and full bacteriological screening—a service which is, unfortunately, rarely available.

We would like to thank Dr J. C. P. Webber and Mr Philip Kingston of Pharmitalia Ltd. for technical assistance and supply of Kelfizine and ampicillin.

Practitioners participating in the trial were Drs A. L. T. Beddoe, A. A. K. Datta, D. M. Cunningham, B. J. F. Coles, Mary T. C. A. Jorro, S. K. M. Chan, Lois M. Leitch, C. B. Grimaldi, A. B. Otlet, R. A. Iles, B. C. E. Aldous, D. C. Jeffrey, P. S. Sinclair, K. L. R. Chu, E. Margaret Dumbell, D. L. Bayley, all of Bristol, and Drs R. W. Morris and M. R. Watts of Thornbury, Glos.

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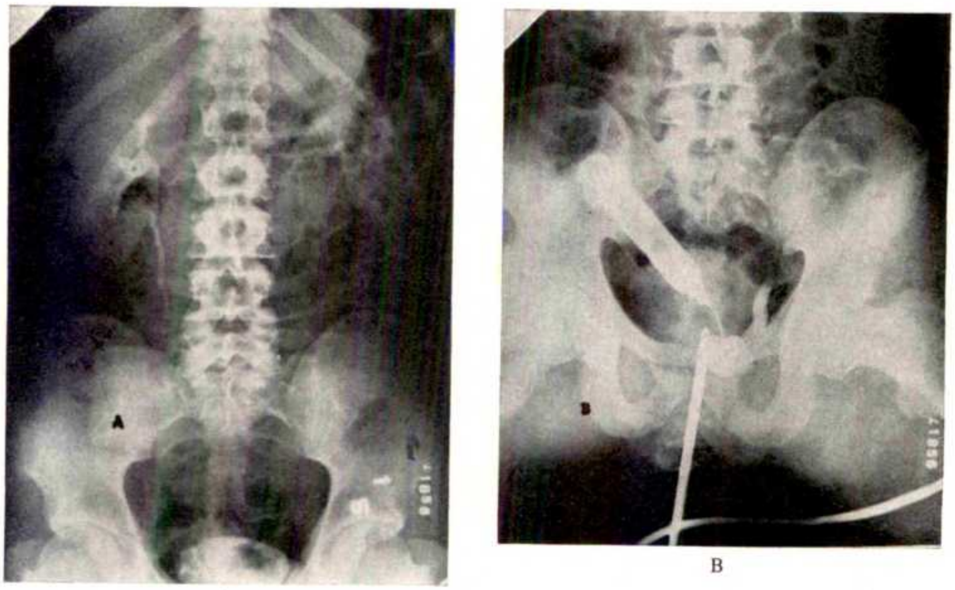
British Journal of Urology (1972), **44**, 110–111

TRANSVESICAL URETEROCELOGRAPHY WITH ENDOSCOPIC CONTROL[1]

By Balfour M. Mount, M.D.

From the Department of Urology, Royal Victoria Hospital, Montreal, 112 PQ, Canada

The difficulty in establishing the diagnosis when a ureter empties outside the bladder in males and cannot be visualised by intravenous pyelography or a voiding cysto-urethrogram has been highlighted by J. Cendron and Cl. Bonhomme (1968). In the absence of an endoscopically demonstrable ipsilateral ureteral orifice, King (1969) has suggested that aortography may be useful by virtue of demonstrating the presence or absence of an associated kidney.



A

B

FIG. 1

A, I.V.P. of a 24-year-old caucasian male with urgency, frequency, and a left supraprostatic mass on digital rectal examination, demonstrating non-visualisation of the left upper urinary tract. B, Ectopic ureterocelograph obtained with endoscopic visual control, the ureter arising from the left seminal vesicle.

Given the presence of a ureterocele in either a normal or ectopic position in association with the absence of upper tract visualisation on the same side, contrast radiography may be achieved by several methods, including (*a*) vasography (a technique which will usually make the diagnosis if an ectopic ureter empties into the seminal vesicle or vas) (Orquiza *et al.*, 1970); (*b*) endoscopic unroofing of the extravesical mass followed by introduction of contrast material (Schmitzer, 1965); and (*c*) needling the mass with introduction of contrast material. A Lyons needle may be used for this purpose.

Schmitzer has accomplished the same end by " spearing the mass with a No. 25 gauge needle tip inserted into a No. 4 ureteral catheter " (Schmitzer, 1965). Transperineal and transrectal needling suggest themselves as two further means of introducing contrast material with, however, the inherent disadvantages of " blind procedures ".

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[1] As suggested by F. Hinman, Jr. in conversation, 1968.

A further diagnostic technique is proposed which offers the advantage of precise visual control. Following cystoscopy and localisation of the cystic mass a panendoscope is inserted and a suprapubic transvesical bladder tap is carried out utilising a 4-inch lumbar puncture needle.

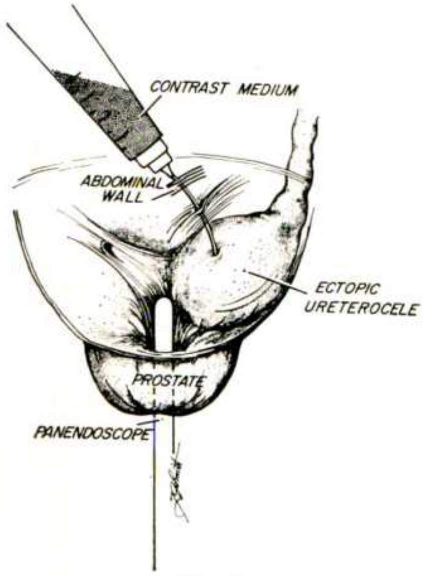

FIG. 2

Transvesical introduction of contrast medium into a ureterocele with the aid of endoscopic visual control.

With the endoscopic control thus afforded the mass may be punctured, fluid aspirated for cytological and bacteriological examinations and contrast medium injected (Figs. 1 and 2). The procedure is safe, simple, and does not require the patient's hospitalisation. It may be particularly useful in male children when the urethra does not accommodate an instrument of sufficient size to accept a Lyons needle or the passage of ureteral catheters.

SUMMARY

A simple technique is proposed for obtaining contrast radiographs in selected cases of ectopic extravesical termination of the ureter and when ureteroceles are associated with non-visualisation of the upper urinary tract on pyelography. It may be particularly useful in children.

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RENAL HAMARTOMA

Angiomyoliposarcoma

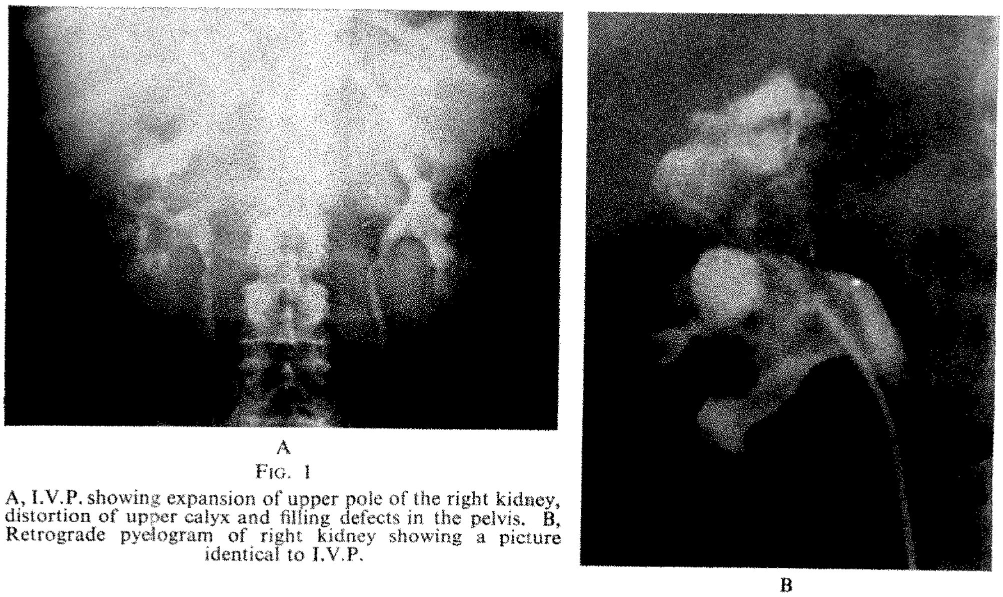
A Case Report

By B. N. COLABAWALLA, F.R.C.S.

St George's Hospital, Bombay

RENAL hamartoma is an uncommon entity. The rarity of the lesion, its occurrence without the stigmata of tuberous sclerosis and its manifestation with hæmaturia, are justifiable reasons for recording a further case.

Case Report.—Mrs D. G., aged 60 years, was referred on 28th May 1969 for intermittent pain in the right loin and hæmaturia of 2 months' duration. The loin pain had started as a dull ache and a week later there was passage of blood in the urine on 2 to 3 occasions. This was succeeded by an episode of severe colicky pain on the right side, associated with profuse hæmaturia, dysuria and increased frequency of micturition. The acute symptoms subsided after a while, but macroscopic and microscopic hæmaturia without pain continued intermittently, for which reason she was referred for further investigations. During the period of the above illness her general health remained satisfactory. The past medical history included a hysterectomy 20 years ago for presumably endometriosis.


A

B

FIG. 1

A, I.V.P. showing expansion of upper pole of the right kidney, distortion of upper calyx and filling defects in the pelvis. B, Retrograde pyelogram of right kidney showing a picture identical to I.V.P.

On examination she was found to be in good general status with a tendency to obesity, weight being 70 kilograms. The blood pressure was 160/90. General examination revealed a distinctly palpable and somewhat tender right kidney. No abnormality was noted clinically in the other systems.

The intravenous urogram suggested an expansion medially of the upper pole of the right kidney. There was distortion of the upper calyceal system and a suggestion of a " break " in the neck of the superior calyx. The pelvis and upper ureter showed multiple filling defects (Fig. 1, A). Urinalysis showed a trace of proteins, 30 to 40 red blood cells, 4 to 6 white cells and a rich growth of *B. coli* on culture. Serum creatinine was 1·4 mg. per cent and the E.S.R. was raised to 44 mm. (Westergren). The hæmogram, serum proteins, glucose tolerance curve, chest radiogram and E.C.G. were within normal ranges. A cystoscopic examination carried out on 6th June 1969

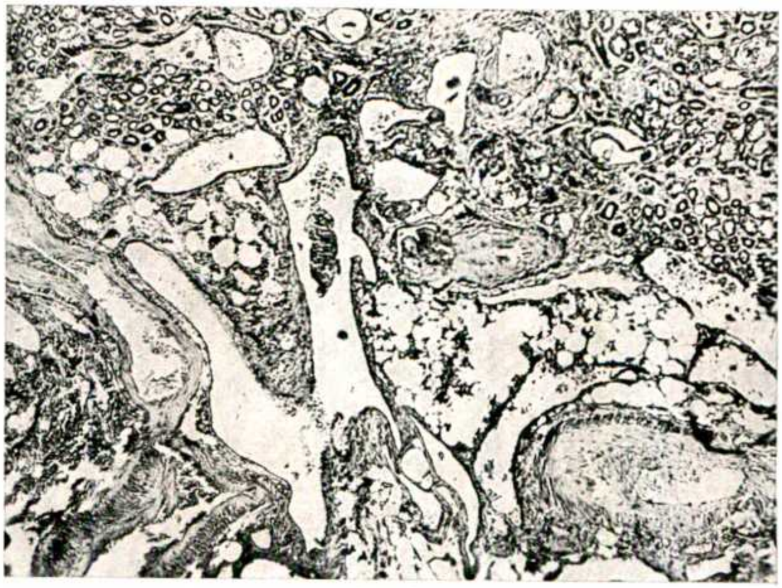


FIG. 2

Photomicrograph showing tumour composed of dilated vascular spaces separated by adipose tissue. A portion of the normal kidney parenchyma is seen. H. & E. × 20.

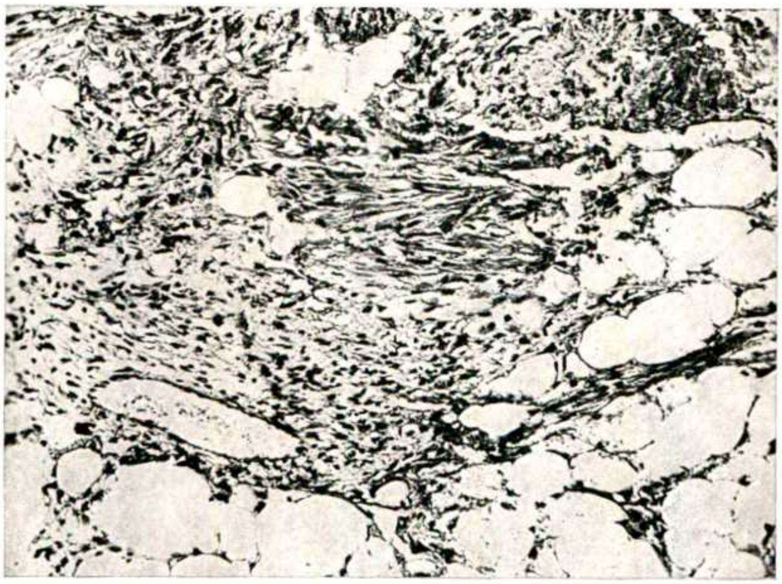


FIG. 3

Photomicrograph showing the smooth muscle component of the tumour consisting of bundles of spindle shaped cells. H. & E. × 120.

revealed no specific features. A retrograde pyelogram on the right side showed a pattern similar to the intravenous urogram (Fig. 1, B). The patient was reluctant to have renal angiography.

A diagnosis of a parenchymal tumour in the upper pole of the kidney was considered. The filling defects in the pelvis and ureter were ascribed to blood clots. An operation for exploration of the right kidney was carried out on 9th June 1969. On exposure of the kidney no distinct tumour mass was palpable, but the medial aspect of the upper pole seemed expanded. The pelvis was full of blood clots. A nephrectomy was carried out.

The histopathological report was as follows:

Gross Observations.—Specimen of kidney (already cut). It shows a rounded hæmorrhagic well-circumscribed area in the cortex measuring 3·5 cm. across with a spongy cut surface. Another smaller ill-defined area is seen in the peripelvic region.

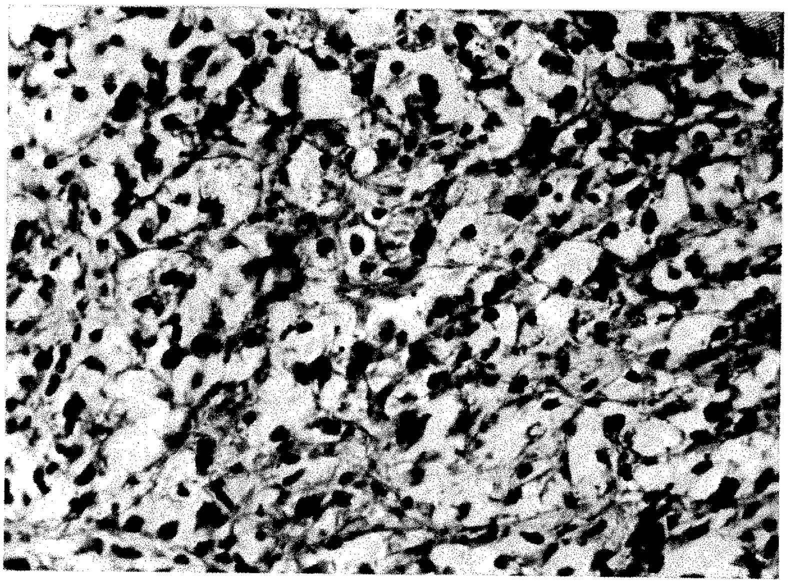


FIG. 4

Photomicrograph showing liposarcomatous area. The cells show an abundant vacuolated cytoplasm. Nuclei are large hyperchromatic and show considerable variation in size and shape. H. & E. ×280.

Microscopical Examination.—Sections from both the tumours show dilated blood vessels surrounded by adipose tissue. A few bundles of smooth muscle cells are also seen. The major portion of the adipose tissue shows small eccentric uniform nuclei. In some sections the nuclei are large, hyperchromatic with bizarre appearance. The rest of the kidney parenchyma shows no abnormality (Figs. 2-4).

Diagnosis.—Angiomyoliposarcoma (hamartomatous in nature).

The patient made an uneventful recovery and was discharged on the 14th day after surgery. Opinions obtained for post-operative radiotherapy suggested that it would be of no value in the case. The patient has attended regularly for follow-up studies and when last seen in January 1971 was in very good health. Subsequent to the surgery, a thorough evaluation for other stigmata of tuberous sclerosis was carried out. Family background for epilepsy and mental illness, X-rays of the skull, neurological and dermatological consultations and fundoscopy all failed to reveal any abnormalities.

DISCUSSION

The term hamartoma is used to describe tumour-like lesions which microscopically are a mixture of mesenchymal tissues such as fat, smooth muscle and blood vessels. Renal hamartomata are seen more commonly in association with tuberous sclerosis, when they are usually small, multifocal bilateral and seen in the young of either sex. Isolated renal lesions are less frequent and are generally larger in size, unilateral, though multifocal at times and occur predominantly in women, particularly in the 6th or 7th decades of life (Allen and Risk, 1965). Seabury *et al.* (1967) mention that approximately 150 cases of renal hamartomata without tuberous sclerosis have been reported. The usual modes of presentation are acute loin pain, appearance of a renal mass and frequently signs of acute blood loss due to severe hæmorrhage within and around the tumour (Heckel and Penick, 1948; Rusche, 1952; Taylor and Genters, 1958). Retroperitoneal hæmorrhage of severe nature has also been reported (Hulse and Palik, 1951; Keshin, 1965). Hæmaturia is less common (Perou and Grey, 1960; Allen and Risk, 1965). Seabury *et al.* (1967) mention that only one-third of the cases present with gross hæmaturia. Fryjordet (1969) reported a case with hæmaturia as a presenting symptom. In the present case, although pain had been a feature, the patient was brought to investigation owing to persistent hæmaturia.

In the isolated renal cases, a precise pre-operative diagnosis is difficult as the clinical and investigative picture cannot be differentiated from that of other varieties of renal tumours. This is exemplified by the case under review in which at one stage, besides the diagnosis of a renal parenchymal tumour, the possibility of an epithelial tumour of the renal pelvis could have easily been entertained in view of the radiological appearance. Khilnani and Wolf (1961) point out that the diagnosis may be suggested by appearance of radiologically translucent area in the tumour due to its fatty content. This observation has not been substantiated in the literature and was not noted in the present case. Renal angiography does not differentiate the lesion from other tumours with vascular pooling (MacDougall, 1960; Seabury *et al.*, 1967).

Considerable controversy exists regarding the origin, pathological features, biological behaviour and malignant potentialities of these tumours. Discussion on these would be out of place here and the reader is referred to the literature. An excellent review is offered by Perou and Gray (1960). The histopathological report of a sarcomatous element in the present case raises the question of the malignant potential of the tumours. Perou and Gray (1960) reported 1 case in their series as being an angiomyoliposarcoma with invasion of blood vessels but without metastasis and also mention a similar case which did not metastasise. They state " not one single instance of metastasis has been recorded when these tumours are found independently of tuberous sclerosis ". Klapproth *et al.* (1959) hold the view that these tumours do not undergo malignant changes though immature and invasive cells may be seen in them. The absence of demonstrable metastasis and maintenance of general well-being in the author's case for 1½ years after surgery, tend to support these views. The other feature to note in the case is the presence of 2 lesions in the kidney, indicating the multifocal nature of the tumour.

As almost all cases simulate a picture of renal parenchymal tumour, the generally employed method of treatment has been nephrectomy. McQueeney *et al.* (1964), though, suggest a frozen section biopsy and conservative resection. Such treatment may not prove adequate when there is a multifocal lesion in the kidney as in the present case.

SUMMARY

A case of isolated renal hamartoma (angiomyoliposarcoma) without stigmata of tuberous sclerosis is recorded. Some aspects of clinical presentation, difficulties in diagnosis and pathological features are pointed out.

I am grateful to Dr M. V. Sirsat, M.D., of the Tata Memorial Centre for the histological report and for the photomicrographs.

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OUT-PATIENT CYSTOSCOPY AND THE SMALL URINARY MEATUS

By ROGER HOLE, F.R.C.S., F.R.C.S.Ed.

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THE use of internal urethrotomy to prevent stricture formation is a safe and well-recognised adjunct to transurethral resection (Emmett *et al.*, 1963). We find this advisable for about 1 in 5 patients undergoing resection with the 27 Ch. Thompson cold punch resectoscope.

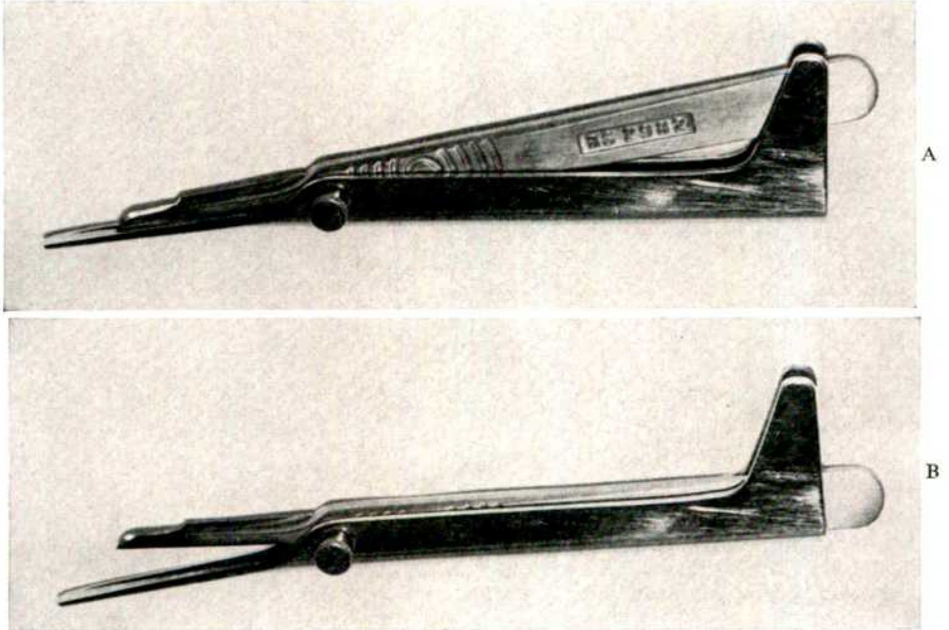

FIG. 1

In about 10 per cent of adult males, the external urinary meatus, although normal in every respect, is too small to allow a cystoscope to be passed easily; enlargement is necessary. The narrow segment lies between 0·75 and 0·25 cm. within the meatus, and can either be incised or dilated. Current practice seems to favour the latter, although dilatation of a normal urethra is certainly theoretically unsound; it may well be harmless in most cases, but occasional patients are encountered where meatal dilatation for cystoscopy has undoubtedly been followed by prolonged dysuria and stricture formation. The time-honoured ventral external meatotomy has 2 disadvantages—the risk of arterial bleeding makes it unsuitable for out-patient use, and because the incision often has to extend proximally to the corona the meatus may be distorted with spraying of the urinary stream.

Since 1968 I have enlarged the narrow segment, when necessary, by a dorsal internal meatotomy performed with a small scalpel. There has been no distortion of the meatus and no problem with bleeding, but it has not always been easy to make the incision to the exact depth required. A robust but simplified version of the Otis urethrotome was needed, and this has now been developed (Figs. 1, A and B). It can be made to cut accurately to 26 Ch. and incorporates a standard Swann-Morton scalpel handle and No. 15 disposable blade.

The Procedure.—The instrument is introduced into the narrow meatus in the closed position (Fig. 2, A). The blade is elevated by closing the handles (Fig. 2, B), and the instrument is then withdrawn, making a single incision in the roof of the urethra. This is no more stimulating under general anæsthesia than dilatation and although initially free venous bleeding may occur, this has persisted after 2 minutes in only 2 of the last 80 cases: both these ceased bleeding within 10 minutes. There have been no other sequelæ.

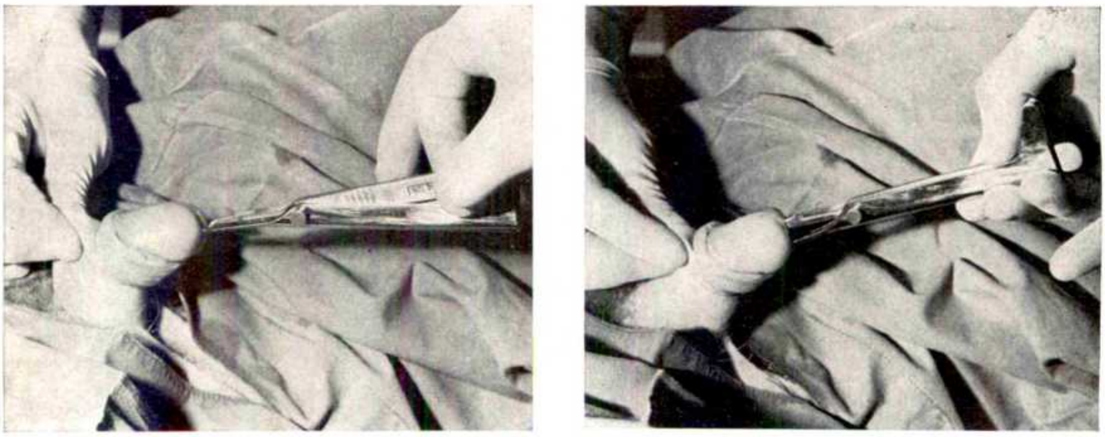
A B

FIG. 2

No follow-up bouginage has been used and the procedure is not intended to produce permanent enlargement of the meatus, but about half of these patients undergoing cystoscopy again later do not require dilatation or meatotomy.

My impression is that there is less post-cystoscopy pain after this procedure than when dilatation has been used.

I would like to thank Mr W. Keith Yeates for much constructive comment, Mr T. Bryson-Smith, Instrument Maker, University of Newcastle upon Tyne, who made the final instrument for me, Swann-Morton (Sales) Ltd. who gave handles and blades, and the Department of Photography, University of Newcastle upon Tyne, who kindly provided the illustrations.

Inquiries about this instrument should be made to the Endoscopic Instrument Company Ltd., 62 Shirland Road, London, W.92 EJ.

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ABSTRACTS OF THE PROCEEDINGS OF THE UROLOGICAL SOCIETY OF AUSTRALASIA

TWENTY-FOURTH ANNUAL GENERAL MEETING, SYDNEY, 1971

President: J. E. BLACKMAN (Sydney)
Hon. Secretary: G. R. GIBSON (Sydney)
Editor: G. F. MURNAGHAN (Sydney)

Technique and Difficulties of Transurethral Resection of Bladder Tumours

By KENNEDY BURNSIDE, F.R.A.C.S.

Alfred Hospital, Prahran, Victoria

Tumours of the bladder can be divided into two groups according to the possibility of eradication by transurethral resection—the distinction between these two groups depends upon the stage of the tumour and not upon its histological grade.

Those patients whose tumours have been eradicated by transurethral resection do very well in comparison with those who have had their tumours eradicated by segmental resection or irradiation of the bladder or by total cystectomy. After transurethral resection there is no disability except their proneness to develop further bladder tumours. After segmental resection there is some diminution of bladder capacity and some risk of spread of the tumour to the abdominal wall. Irradiation may only be used once and patients who have been irradiated may have cystitis or proctitis. Total cystectomy carries a significant mortality with the morbidity and problems of urinary diversion.

Intravenous pyelography and double contrast cystography are necessary preludes to transurethral resection in order to assess the size, position and the smoothness or otherwise of the tumour and the presence or absence of ureteric obstruction. Endoscopic examination of the tumour and bimanual assessment under the anaesthetic must be undertaken before resection is commenced.

The tumour should be resected rather than coagulated so that biopsy material is available: this may be of particular importance with recurrent tumours which require careful distinction from inflammatory granulomata.

Relaxant anaesthesia is essential for prevention of accidental perforation of the bladder wall and a high cutting current should be used to facilitate precision of resection, which should begin at the edge of the tumour and end with the pedicle. Resection is continued until either bladder muscle is seen throughout the area of the tumour or a hole is made in the bladder wall. Such perforation of the extra peritoneal part of the bladder is not dangerous and usually requires no further treatment than prophylactic antibiotics. Perforation of the intra peritoneal part of the bladder should be avoided because it requires laparotomy and suture.

Familiarity with the resectoscope is essential and may be acquired by using this instrument for routine examination of the bladder. Large tumours that almost fill the bladder cavity may cause difficulty in resection but may be aspirated through a suction syringe or resected in stages on separate occasions.

Ureteric obstruction by oedema after resection of tumour near to the ureteric orifice may become dangerous if infection supervenes and prophylactic antibiotics are thus indicated.

Segmental resection is a better alternative to transurethral resection when tumours near the bladder fundus are inaccessible or when there is ureteric obstruction.

When all the evidence is available the tumours may be determined as obviously resectable, obviously not resectable or of doubtful suitability for resection. The doubtful group should be given a trial of resection. If this appears to be completed satisfactorily then careful reassessment would be required after an interval of three months and any suspicion of recurrence should be confirmed by further biopsy.

The Results and Failures of Transurethral Resection of Bladder Tumours

By DAVID GUNTER, F.R.A.C.S.

Alfred Hospital, Prahran, Victoria

A series of 470 patients with bladder tumours treated by endoscopic resection have been available for review after a six year period of follow up. Histological grading of the tumours was as follows:

Grade I	83
Grade II	157
Grade III	107
Grade IV	115
Doubtful Grade	8

The mortality rate amongst 240 patients with either grade I or grade II tumours was 20% during the six year period. The recurrence rate amongst single and double tumours was 46%. Almost half of these recurrent tumours presented at the original tumour site and of these 80% occurred during the first year of follow up and 8% of them were found to be of higher grade than the original tumour. Sixty-eight per cent. of tumours occurring, other than at the original tumour site, presented in the first year of follow up and 14% were of higher grade. The recurrence rate amongst Grade I and Grade II multiple papillary tumours was 85% and approximately one quarter of these were of higher grade of malignancy than the primary tumour.

The mortality rate amongst 107 patients with grade III tumours was 41% at six years. Of 19 patients without recurrence three had died, whilst 41 of 88 patients with recurrence had died. Forty-three patients of the entire grade III group were subjected to external irradiation therapy.

Of 115 patients with grade IV tumours, only four were well and without recurrent tumour after three or more years of follow up. Nine patients with recurrence survived three years but only two patients with recurrence survived for five years. Thirty-seven patients had been subjected to external irradiation therapy, 25 to total cystectomy, two had undergone partial cystectomy and three patients were found to be inoperable at exploratory surgery.

Extended Partial Cystectomy in the Management of Bladder Carcinoma Rationale and Case Selection

By N. J. Bonnin, M.S., F.R.C.S., F.R.A.C.S.

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Partial cystectomy if carried out according to the common text book description does not conform to the usual standards required of an operation for removal of a cancer; it allows for the risk of contamination of the wound by cancer cells, tissue excision is not extensive, lymph node dissection is not performed and the subsequent bladder capacity may be inadequate. Improvements in technique of partial cystectomy have been developed to overcome these objections and consequently the scope of the operation has been extended.

Partial cystectomy is applicable to localised bladder tumours which occupy an area of less than half of the bladder wall. Complete excision of such tumours is possible because papillary type tumours extend through the bladder wall towards the perivesical fat with little tendency to spread laterally. The operation is contraindicated in the treatment of multiple papillomatosis, carcinoma in situ and diffuse, poorly localised squamous or anaplastic tumours.

Endoscopic resection is the preferred method of ablation of localised bladder tumours wherever possible but partial cystectomy is indicated by inability to completely destroy a localised tumour.

The extent of excision has been arbitrarily limited to one half of the bladder. The risk of contamination by tumour cells at the time of surgery has been minimised by irrigation with a one per cent solution of silver nitrate and then by total destruction of the whole tumour surface by diathermy, before partial cystectomy is performed. Whenever possible the diathermy is applied as a preliminary endoscopic procedure but if this should prove impossible then the fulguration is carried out as an open procedure with careful isolation of the bladder which is then closed and irrigated with silver nitrate solution before proceeding to partial cystectomy. Perivesical excision of contiguous tissue, viscera and glands is carried out with partial cystectomy in a comparable manner to total cystectomy.

In bladder reconstruction after partial excision, care is taken to obtain a spherical shape. The edges are approximated by whole thickness interrupted sutures because continuous suturing tends to inhibit elongation of the scar and restrict the bladder capacity.

Pre-operative assessment, correction of any bladder neck obstruction, proper case selection and attention to all details of technique are essential for the effective use of partial cystectomy. With these essentials the procedure has been used as a desirable alternative to total cystectomy or local irradiation in the treatment of localised but extensive tumours some of which have penetrated the bladder wall and show anaplastic change.

Post-operative bladder function has been satisfactory with patients restored to normal health and activity.

Extended Partial Cystectomy in the Management of Bladder Carcinoma: Technique and Results

By John S. Jose, M.A., F.R.C.S., F.R.A.C.S.

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After preliminary transurethral resection of the tumour and the instillation of one per cent solution of silver nitrate to minimise wound seeding, the bladder is exposed through a lower paramedian incision and fully mobilised. If the tumour lies near to the trigone then mobilisation may include the division of the lateral vesicular pedicles and the separation of the space of Denonvillier as included in the procedure of total cystectomy.

The preliminary transurethral resection facilitates identification of the segment of bladder to be removed. Regional pelvic lymph nodes, perivesical fat, portions of the lower ureter, prostatic capsule, seminal vesicles, cervix, uterus and anterior vaginal fornix may all be included in the resected tissue.

Simple open ureteric re-implantation has proved trouble free provided that any obstruction to bladder outflow is relieved at the time of partial cystectomy. Closure of the bladder defect is accomplished in two layers except at the bladder neck where difficulty of access requires preliminary placement and subsequent tying of through-and-through sutures between the apex of the bladder repair and the bladder neck. The closure is designed as far as possible to reconstitute a spherical bladder of maximum capacity.

The use of this technique for the treatment of localised infiltrating bladder tumours in 65 patients has not been followed by significant morbidity or reduction of long term survival even when ureteric re-implantation and prostatectomy have been included in the extended partial cystectomy.

Cytology of Bladder Cancer

By W. G. E. Straffon, F.R.C.S.

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In the period 1965-70 more than 1,200 cytological studies were carried out on urine samples from approximately 600 patients, and an analysis has been carried out of the results of cytological examination of 313 samples of bladder urine taken at the time of cystoscopy. Cytological grading was compared with endoscopic appearances, and histological grading of any tumours found.

Thirty per cent. of patients with tumours showing grade I histology had negative cytology, and 44% had grade I cytology. Correlation of histological grading with cytological grading of the bladder tumours was more significant amongst the malignant tumours.

Cytological studies gave a false negative rate of 17% and forecasts of histological grading on the results of cytological study were only 50% accurate.

Malignant disease was diagnosed falsely in 48% of the cytological examinations. Further scrutiny suggested that inflammatory lesions in the bladder did not appear to influence the results of cytological study. Almost one half of the false positive results related to cytological study (grade I) of sheets of almost normal transitional epithelium which could have been detached by the cystoscope. Almost 10% of patients having false positive cytological results were found to have endoscopic evidence of recurrence of bladder tumour within one year of false cytological presentation.

Local Chemotherapy in Bladder Cancer

By G. R. Gibson, LL.B., F.R.C.S., F.R.A.C.S.

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The local application of chemotherapy subjects the whole bladder surface to a high concentration of the agent used so that multifocal tumours and exfoliated free cells from existing tumours may all be affected.

Weekly intravesical instillations of 60 mg. Thiotepa dissolved in 50 ml. of distilled water were given for four successive weeks to each of 32 patients with proven bladder tumours. The course was repeated in any patient when cystoscopic review showed inadequate response. A single instillation of 60 mg. of the drug was used in each of six patients.

Twenty-three patients with stage T1, none invasive, well differentiated tumours became tumour free or were improved by this treatment during an average follow up period of 28 months. Nine patients with stage T2, invasive and less differentiated tumours were either unchanged, deteriorated or died during an average follow up period of 12 months after treatment.

In four patients, tumours subsequently developed in the posterior urethra despite disappearance or improvement in the bladder tumours following Thiotepa.

Significant bone marrow depression occurred in each of four patients who had received more than one course of treatment.

Intravenous Methotrexate in the Treatment of Advanced Bladder Cancer

By G. D. Burfield, F.R.C.S., F.R.A.C.S.

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Chemotherapeutic agents have not generally been successful in the control of malignant change in urothelium. Five fluoro-urocil and Methotrexate are the agents which have been most commonly used but experience with Methotrexate administered orally or by intra-arterial perfusion has been unimpressive and there have been no reports of the intravenous administration of this drug in the treatment of bladder cancer.

This paper reports the results of a pilot study of the use of intermittent intravenous Methotrexate in the treatment of advanced bladder cancer at the Royal Marsden Hospital in London.

Twenty-six patients were accepted for the trial and all were treated on an out-patient basis. Initial assessment directly related to any symptoms, physical or radiological signs which could be used as indices of clinical response.

Extreme caution was required in the use of the drug in the presence of impaired renal function.

One hundred mg. of Methotrexate were given as a single intravenous dose at intervals of one to two weeks, according to renal function. The dose was reduced to 50 mg. as a trial or maintenance dose if function was impaired. Each patient was given 40 mg. Frusemide orally at the time of the injection so that the usual route of excretion of the Methotrexate would be hastened and the toxicity would be minimised.

Six of the 26 patients in the trial showed both symptomatic and objective signs of tumour regression. Seven patients had some temporary symptomatic improvement but no response was noted in the remaining 13 patients. Remission was only temporary, the longest period being six months. No deaths were attributable to the treatment, though toxicity was problematical in the initial stages of treatment until the individual drug dosage was stabilised. It was thought that toxicity of Methotrexate was much less during intravenous administration in comparison with other routes.

Following the initial study a second series of 9 patients have been treated in a similar manner and none have shown any clinical response.

The results of the use of intravenous Methotrexate in bladder cancer were no better than those previously obtained with other chemotherapeutic agents.

Urinary Diversion following Total Cystectomy for Carcinoma of the Urinary Bladder

By G. B. Ong, C.B.E., F.R.C.S., F.R.A.C.S.
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From 1949 to 1971 a total of 244 cases of carcinoma of the urinary bladder were admitted to the University Surgical Unit, Queen Mary Hospital, Hong Kong. Seventy-two of these patients underwent total cystectomy and required some form of urinary diversion. In the early part of this period—from 1949 to 1963—ureterosigmoidostomy was the method of urinary diversion. The immediate results were poor as were the late results and no patient survived five years. This form of urinary diversion has not been carried out since 1964 and construction of an ileal conduit has been preferred in patients that underwent total cystectomy. The results of ileal conduit were much better although the mortality rate was still high.

Rectal bladder was used in two patients, one of them died of metastases five years after the operation, whilst the other is still alive and well six years after the surgical treatment.

A colonic conduit was fashioned in one patient after the failure of colocystoplasty.

Because of the difficulties encountered with a patient with ileal cystoplasty carried out in 1958, colocystoplasty has been resorted to and within the period of seven years (1963-1970) 30 such operations were performed. The procedure failed in two patients and diversion was converted to ileal conduit in one and to colonic conduit in the other. The remaining patients have continued with colocystoplasty; eleven patients are still alive and two of these have survived more than five years following operation.

The functional results of colocystoplasty have been excellent in some patients and good in others, but one patient was incontinent.

Because of chloride absorption and the possibility of the development of acidosis, it was considered that the stomach might be a better organ for bladder replacement. During the last three years experimental bladder replacement has been carried out in dogs and the results have been found to be satisfactory. There is no evidence of absorption of the chloride.

Five patients with bladder carcinoma have undergone total cystectomy during the past year using gastrocystoplasty as the method of reconstruction. Three patients have survived and their functional results are presently being studied.

Management of the Terminal Patient with Prostatic Cancer

By R. H. Farnsworth, F.R.C.S.Ed., F.R.A.C.S.

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Though oestrogen therapy, either alone or in combination with castration, is a well established form of treatment of patients with metastatic prostatic cancer it may be followed on rare occasions by accelerated clinical deterioration. In four patients with such deterioration androgen therapy was prescribed. A dramatic remission occurred in one patient, and two further patients had precipitous falls in their levels of serum acid phosphatase but without clinical improvement.

Cryostatic hypophysectomy successfully relieved severe widespread bone pain in three out of four patients who had failed to respond to previous hormone therapy and local radiotherapy. Such dramatic relief of the symptoms was not accompanied by any postponement of death from tumour progression.

Post Prostatectomy Rectovesical Fistula

By P. Harbison, F.R.C.S., F.R.A.C.S.

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Development of a fistulous communication between the urinary and faecal tracts after prostatectomy is a disastrous condition, the management of which is poorly documented. The complication usually follows a difficult enucleation of the prostate or an unsuspected carcinoma of the gland or excessive use of the diathermy.

Three patients with rectovesical fistula were presented as follows:

(1) One patient developed a fistula following retropubic enucleation prostatectomy. The fistula closed following a period of indwelling urethral catheter drainage combined with transrectal suture.

(2) A fistula developed in a paraplegic patient as a complication of transurethral resection of the prostate. This fistula was closed successfully through a perineal approach.

(3) A fistula which developed after retropubic enucleation prostatectomy was closed through a "Kraske" approach with the removal of lower sacrum and coccyx to allow for mobilisation of the rectum and closure of the fistula.

Surgical treatment of postprostatectomy rectovesical fistula could be satisfactorily staged as follows:

(*a*) Anal dilatation and transrectal suture.

(*b*) Indwelling urethral catheter drainage for a four week period.

(*c*) Defunctioning colostomy.

(*d*) Closure of the rectovesical fistula by the perineal or "Krascke" approach with subsequent closure of the colostomy.

Treatment of Post Prostatectomy Haemorrhage

By L. I. Parton, M.B., B.Sc., F.R.C.S.

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Haemorrhage following Hryntschak prostatectomy has been considerably reduced by the insertion of one transverse suture, and one "semicircular" suture to enclose the posterior half of the prostatic cavity. Each of these sutures is inserted behind but tied in front of the catheter. The stitches are passed through a small loop of wire which projects from the catheter. The wire passes down the lumen of the catheter and emerges from its distal end, so that when removal of the catheter is required diathermy application to the distal end of the wire ensures that the catgut sutures in the prostatic region are cut and the bladder neck opens up. After open prostatectomy or transurethral prostatic resection continuous saline irrigation is used through a "Kinder" catheter. If haemorrhage is considered to be excessive and before clots have formed then the saline irrigation is replaced by a rapid irrigation with a solution of 1 in 10,000 silver nitrate. This method is simple and will rapidly and dramatically produce control of haemorrhage within 30 or 60 minutes at which time saline irrigation is resumed. Silver nitrate irrigation has been useful in the prevention of major post operative complications due to haemorrhage after prostatectomy.

Pathology of Testis Tumours

By Édmond Hirst, D.C.P., M.C.P.A.

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Testicular tumours occur in about 2·5 males per 100,000 of the population. The incidence is thus about one third that of bladder tumours. In Australia between 150 and 200 new testis tumours present each year. There is a marked racial difference in the incidence, the commonest being in Caucasians, the rarest in negroes with an intermediate incidence in people of mixed race. In the United Kingdom there is a rural preponderance over the cities. In children, the commonest tumour is an orchioblastoma and though teratomas do occur they are almost always benign under the age of two years. Seminoma is rare in childhood then usually occurs in undescended or maldescended testes. Embryonal carcinoma is a rare tumour in children.

In about 40% of seminomas granulomatous inflammation is present. The patients who die of metastatic seminoma are rather few in number and only 60 to 70% of them show seminoma in the metastases—the remainder have metastases in the form of differentiated teratoma, embryonal carcinoma or even choriocarcinoma.

The spermatocytic seminoma is now thought to be a completely different tumour to the classical seminoma. It is usually smaller with a more mucoid cut surface and on histological study shows sheets of cells many of which are small and resemble lymphocytes but are thought to be maturing into spermatocytes. This tumour occurs in patients 20 years older than the average age for presentation of a seminoma and has a better prognosis.

The teratoma is usually characterised by areas of haemorrhage and cysts. Complete undifferentiation in a teratoma is characterised by indistinction of the cytoplasm of the cells so that the nuclei appear to lie in a syncitium. Such embryonal carcinoma could be considered to be the most undifferentiated of the germ cell tumours because one individual cell can produce a teratoma. Cytoplasm and nuclei of these cells show the same organel structure by electron microscopy as do the germ cells themselves.

Teratomas can be completely differentiated but full differentiation can be trusted only in children and women.

Choriocarcinoma is an undisputed tumour arising from germ cells. It is very rapidly fatal when it occurs in the testis in the pure form. When foci of choriocarcinoma appear in other tumours prognosis is worse than the tumour would be without the choriocarcinoma but it is not inevitably fatal.

A small tumour occasionally presents in a small testis in the form of an orchioblastoma or adenocarcinoma of the infant testis which is differentiated from germ cells and may be referred to as the yolk sac tumour or the endodermal sinus tumour. These carcinomas of the infant testis when present under the age of 14 months of age are uniformly benign. In older children and in adults the tumour is quite often fatal.

Though the combination of teratoma and seminoma is well known it is not often appreciated that there are foci of seminoma in about 12% of teratomas.

Interstitial cell tumours occur in children, men and old dogs, with sexual precocity in children and gynecomastia in adults. The Sertoli cell tumour also arises from stromal cells. This tumour is often called the male arrhenoblastoma.

The Place of Radiotherapy in Testicular Tumours

By L. Atkinson, F.R.C.S., D.M.R.T.,
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One hundred and forty cases of germ cell tumours of the testis presented at the Departments of Radiotherapy in these hospitals between 1955 and 1969. There were 72 seminomas, and 68 cases of other pathology including 17 mixed teratoma-seminomas, one pure trophoblastic tumour and several teratomas containing some trophoblastic elements. In addition to the germ cell tumours there were three lymphomas, three soft connective tissue sarcomas, two cases of disputed pathology. Seven patients were referred with metastatic disease after initial treatment in other centres.

One hundred and thirty-eight patients received surgical treatment by simple orchidectomy which was sometimes extended into the pelvis for removal of palpable lymph nodes: two patients underwent orchidectomy with extended lymphadenectomy. Two patients received no surgical treatment.

Fifty-five of the seminomas were Stage A (confined to testis); ten were Stage B, (spread along the spermatic cord or into abdominal lymph nodes); one was Stage C (distant metastases) and three cases were inadequately staged. In the group of tumours other than seminoma 51 were Stage A, seven Stage B, and 13 Stage C. After a simple orchidectomy the routine programme comprised 4,000 rads of irradiation limited to the para-aortic region but the fields were extended according to the limits of the disease or when there had been surgical interference with the scrotum.

The observed overall survival rate including all cases of death during a five year period was 68% for the entire series, 86% for the seminoma cases and 51% for the group of other pathology. Five year survival for Stage A tumours was 96% in the seminoma group and 63% in the tumours other than seminoma.

Of 17 cases of mixed teratoma-seminoma three died during the first year of follow up, the remainder are well and surviving between two and eleven years after treatment. The patients with Stage A teratoma who survived (63%) have all retained their potency and many have sired children after orchidectomy and irradiation.

Criteria for possible selection of patients with teratoma who should be recommended for lymph node dissection are being sought. It does not appear that such radical surgery should be offered to patients with mixed teratoma-seminoma or with teratomas of a similar type and stage to those which allowed for a 63% survival rate in the present series.

Survival up to three years of patients with pulmonary metastases from teratoma has followed treatment by orchidectomy, cytotoxic therapy and irradiation to include a large volume of lymphatic tissue in a similar programme to that advocated for the treatment of Hodgkin's disease.

An Unselected Series of Patients with Testicular Tumours—Results of Treatment of 100 Cases

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This series of 100 patients with testicular tumour presented in Christchurch between 1954 and 1968 and represents a regional incidence rate of 3·25 cases per 100,000 of the male population of the region per year.

All patients have been routinely subjected to chest radiography, pyelography and pregnancy hormone tests. In recent years lymphography has been applied routinely and inferior vena cavography has been available when indicated.

In 85 patients the disease was localised to the scrotum, in eight patients there were palpable abdominal swellings and in seven patients the disease had spread beyond the abdomen.

Pathological examination showed that 50 tumours were seminoma, 24 malignant teratoma, 14 combined tumours, seven trophoblastic teratoma and five were miscellaneous varieties.

A uniform policy of management has included orchidectomy with high ligation of the spermatic cord at the deep inguinal ring. Orchidectomy is followed by radiotherapy to the regional nodes using wide field radiation therapy in moderate dosage for patients with seminoma and higher dosage radiation of more restricted fields in patients with other tumours. A retroperitoneal lymph node dissection has not been routinely carried out but a most important feature of management has been the deliberate pursuit and resection of early symptomless pulmonary metastases in patients presenting with stage I teratoma or combined tumour. Such resection of pulmonary metastases which were not present at the time of initial treatment has been carried out in seven patients with teratoma and six of these patients have survived.

Multiple chemotherapy regimes have been used for more advanced cases but have proved disappointing.

Of the 100 patients seen in the 13½ year period under review, 61 are alive and disease free at periods of follow up between three and 13½ years. Thirty-seven patients are dead and two lost to follow up.

The overall survival rate of 61% includes a 74% survival of all cases of seminoma with 81·4% survival of stage I seminoma cases. In the teratoma group survival overall is 53% which includes the survival rate of 64·5% of stage I teratoma cases.

Of seven patients with trophoblastic teratoma five are dead.

An analysis of the postmortem findings of the 37 patients who died would lend support to the desirability of selecting particular patients for retroperitoneal lymph node dissection by the use of improved means of assessment of the actual status of the retroperitoneal lymph nodes at the time of diagnosis. The analysis failed to suggest any sound basis upon which the patient could be spared irradiation treatment to the regional lymph nodes.

Testicular Tumours

By H. Thomas, F.R.C.S., F.R.A.C.S., F.A.C.S.

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Over a ten year period 54 testicular tumour cases have been treated in these hospitals. The largest pathological groups comprised seminoma (22 cases) and teratoma (25 cases). Sixty-two per cent. of the patients in the series had had symptoms for two months or longer before admission to hospital, whilst in 26% of the patients some delay in diagnosis had been caused by the mistaken diagnosis of epididymo-orchitis.

The most common presenting symptoms were swelling and/or heaviness of the testis (57%), or pain and swelling of the testis (36%). In 18% of the patients the family doctor had made a clinical diagnosis of hydrocoele and had attempted aspiration. One quarter of those patients who received antibiotic therapy in the belief that the scrotal swelling was of inflammatory origin showed an apparent clinical improvement.

In 24% of the series antecedent history of injury to the testis was obtained; 77% of these patients denied feeling pain. This finding was in marked contrast to the usual history of pain subsequent to injury to a normal testis.

The standard initial treatment of these patients comprised orchidectomy with high ligation of the spermatic cord at the level of the internal inguinal ring. Each of the patients with seminoma of the testis received radiotherapy to cover a field from the aortic bifurcation to the diaphragm. One patient with teratoma of the testis underwent retroperitoneal lymphadenectomy and subsequently developed pulmonary metastases but has survived three further years following lobectomy. When attempted aspiration of the scrotum had preceded orchidectomy then excision of that half of the scrotum was carried out.

The survival patterns heavily favoured the seminoma patients as a major group.

A New Method of Bladder Neck Repair for Urinary Incontinence

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The internal urethral meatus is the point at which urine escapes from the bladder and which is occluded by the surrounding muscle of the urethra. Though there is debate concerning the function and configuration of this " internal sphincter," reconstruction of the sphincter around the meatus has restored continence to five female patients who had leakage of urine with small continence capacity bladders and despite regular micturition by day.

In three patients the vesico-urethral segment of urethral ectopic ureters had been excised or incised from within the bladder; in a fourth patient the bladder neck was incompetent following penetrating injury and in the fifth patient leakage occurred following repair of a congenital recto-urethral fistula. In each of these five patients the internal meatus was patulous and larger than normal and permitted leakage of urine into the urethra when the bladder was partly filled and on exertion of the patient.

Such incontinence could be due to disruption of the urethrotrigonal muscle complex with either over-stretch or division of the muscle rings of the trigone which form a flat platform of the trigone but embrace the sides and anterior walls of the urethra above and below the internal urethral meatus. Active contraction of the torn slings may perpetuate the dehiscence and open rather than close the urethra.

An operation has been devised to repair the urethrotrigonal sphincter mechanism by reducing the lumen of the internal urethral meatus by converting the circular trigonal muscle rings into a bipennate keel in order to reduce the effective circumference of the rings and alter their action from constriction to that of pubic pull of the posterior lip towards the anterior wall.

The trigone and internal meatus are exposed through a suprapubic incision in the bladder wall. The trigone is stretched laterally with guy stitches which temporarily underrun the ureteric orifices. The mucosa is incised in the midline from the level of the ureteric orifices into the urethra through the lax bladder neck and widely undermined on each side, especially to the mid lateral region on the bladder neck. The whole thickness of the muscle coat of the trigone is incised with the incision veering towards the side of the suspected deficiency in the bladder neck region. The cut edges are turned posteriorly to bipennate and keel the trigone and internal meatus by the use of a Cushing suture of 4/0 chromic catgut on a 20 mm. atraumatic suture. Two more rows of Lembert sutures are then inserted, starting from the cranial end to further elongate the keel and reduce the lumen of the meatus. In these two rows, the most caudal sutures are inserted using a 16 mm. 11/16 circle Denis Browne needle. With this needle good bites can be achieved into the lateral walls of the bladder neck especially if traction is applied to the preceding stitch to create a shoulder effect on each side. These bladder neck stitches after insertion are best left long and untied until the last stitch is suitably placed. Then they are tied and cut one by one and as they are drawn together any tension can be reduced by division of extra-urethral attachments in the lateral aspects of the vesico-urethral structures. Finally the mucosa is trimmed and sutured with a continuous running stitch of catgut. The urethral lumen at the bladder neck is reduced as much as possible by the keeling procedure and in no instance has this proved to be too small.

The five patients have all been improved by this operation and three are completely cured. Two patients can remain dry for two hour periods and are dry for most of the day provided that micturition by the clock is adhered to.

External Urethroplasty for Treatment of the Urethral Syndrome in the Female

By Francis H. Richardson, M.D.

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Fourteen hundred and fifty patients exhibiting the usual group of symptoms associated with the urethral syndrome were treated over a seven year period by excision of a ring of peri-urethral tissue from around the posterior half of the distal one-third of the urethra. The surgical approach was through a transverse incision in the vaginal mucosa along the hymenal ring. The vaginal mucosa was reflected off the distal urethra and replaced back into its original position after excision of peri-urethral fibro-elastic tissue. There were 275 girls and 1,175 women in this series.

The tissue to be removed is distal to the internal and external urethral sphincters but is not characterised by any features detected on palpation, calibration of the urethra or by cinecysto-urethrography. In this series abnormal bladder function was determined by the single parameter of average urine flow rate. In each patient the bladder was filled with water to capacity by gravity and the duration of voiding was timed and the bladder then checked for residual urine. An increase in the average flow rate after surgery seemed to correlate directly with improvement in urinary symptoms.

No patients were made worse or became incontinent after urethroplasty and the clinical results were satisfactory in 93% of the series, whilst 5% of the patients were improved and 2% were unchanged. Seven per cent. of the patients in the series required an occasional urethral dilatation post operatively. Two per cent. of the patients had surgical treatment repeated after failure to show any permanent improvement in the average urine flow rate. Incompetence of the bladder neck with decompensation of the bladder wall as a result of long standing distal urethral obstruction are believed to be the factors responsible for lack of improvement.

The improvement in patients with recurrent cystitis is attributed to the faster urine flow rate with more adequate washout of bacteria in the urethra.

In patients with an irritable bladder syndrome a decrease in the urethral resistance permits the bladder muscle to relax, and to tolerate larger volumes of urine. The elimination of referred pain from the bladder and the dyspareunia associated with chronic urethritis are extra benefits of urethroplasty.

Carcinoma of the Renal Pelvis

By G. B. Ong, C.B.E., F.R.C.S., F.R.A.C.S.
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Carcinoma of the renal pelvis is an uncommon tumour. The University Surgical Unit at the Queen Mary Hospital has an attendance at the urological clinic of over 4,000 patients a year, but has only treated 13 patients with carcinoma arising from the renal pelvis during the past 13 years.

There were six male and seven female patients whose ages ranged from 26 to 74 years, with an average age of 59 years.

When first seen it was found that the tumour involved the bladder in three patients, with lymphatic involvement in three, liver involvement in two and infiltration of the renal capsule with skin metastases in one patient.

Histological studies of these 13 tumours showed that the carcinoma was transitional cell in nine, squamous cell in three and anaplastic in one. Of the three cases in which the bladder was involved two were found histologically to be transitional cell tumours whilst the other was anaplastic. Three cases of squamous cell carcinoma were associated with stones and infection. Of the nine cases of transitional cell carcinoma of the renal pelvis, two had stones in the kidney and five were associated with infection.

Clinically, haematuria was the most common complaint and it occurred in eight patients. A mass was palpable in three patients and loin pain was the chief complaint of two patients. The tumours presented on the right side in six patients and on the left side in seven cases.

Intravenous pyelography was characterised by absent function in seven cases, filling defect in three, hydronephrosis in two and distortion in one. Each of these patients underwent extensive investigations and though lymphangiograms showed no abnormality it was found at operation in three patients that the lymph nodes contained metastases. Renal arteriography was carried out without positive results except in one case which showed displacement of vessels due to hydronephrosis. It would appear therefore that these investigations are of little or no value.

Nephroureterectomy was the treatment used in the majority of cases. The nephrectomy was done with the standard kidney incision and was then extended right down into the pelvis and a cuff of the bladder was excised at the same operation.

There was no operative death, but the five year survival rate was poor. Ten patients died of the disease within five years, two are still alive at four years after operation and one case with squamous cell carcinoma is alive five years after initial operation but with residual disease despite two courses of radiotherapy.

Carcinoma of the renal pelvis as seen in Hong Kong is not common. The incidence is probably much higher than one expects because some cases of gross hydronephrosis thought to be uncomplicated may in fact contain carcinoma.

Endocrine Aspects of Renal Carcinoma

By G. F. MURNAGHAN, M.D., Ch.M., F.R.C.S.

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Sydney, N.S.W.

Hormone therapy has been applied in an attempt to control distant metastases from renal carcinoma in a series of eleven patients.

Three male and three female patients with ages ranging from 26 to 71 years received intramuscular, oral or combined therapy with ethynodiol diacetate in a daily dose of 50-60 mg. Four of these patients had been treated by nephrectomy and two by irradiation therapy of the primary lesion. Symptomatic relief was obtained in two patients with pain; in only one patient did it appear that metastases were controlled and in none of these six patients was there regression of tumour.

The seventh patient of the series was female and underwent nephrectomy with post operative irradiation for hypernephroma at the age of 66 years. Ten months after operation she presented with metastases in the lungs, spine and scalp. The metastases did not regress but showed no obvious progression whilst she received daily medication with prednisone 30 mg. and ethynodiol diacetate 15 mg. during a short period of follow up.

In four patients the administration of Megestrol (B.D.H.) or Melengestrol (B.D.H.) sometimes with testosterone supplement was thought to be of definite subjective benefit but the effect was not dramatic. In one of these four patients transient regression of metastatic disease occurred at a time when it was thought that the testosterone supplement may have caused accelerated tumour progression.

Analgesics and Carcinoma of the Kidney

By J. STUART TAYLOR, F.R.C.S., F.R.A.C.S.

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A 5 year retrospective study has been made of the relationship between carcinoma in the urinary tract and analgesic nephropathy.

The incidence of carcinoma of the renal pelvis was 160 times higher in patients with histological or radiological proof of analgesic nephropathy, than it was in patients with radiological evidence of renal disease. The incidence of similar tumours in patients with non-obstructive pyelonephritis was 17 times higher than that found in patients without radiological evidence of renal disease. In analgesic nephropathy the overall incidence of tumour of the renal pelvis was increased to 28% of all tumours of the kidney but there was a reversal of the usual sex incidence of such tumours to 5·5 female to each male so that the incidence of renal pelvic tumour paralleled the sex incidence of analgesic nephropathy in the population.

Frank painless haematuria was found to be of sinister clinical significance in patients with analgesic nephropathy: eight of twelve patients presenting with this symptom were found to have carcinoma of the renal pelvis. No relationship between smoking and carcinoma of the renal pelvis was demonstrated but it was clearly shown that the changes of analgesic nephropathy preceded the development of such tumours in four patients.

Simplified Renal Hypothermia as Adjunct to Conservative Renal Surgery

By M. JULIAN METZNER, F.R.C.S.Ed., F.R.C.S.

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Melbourne, Victoria

A concise understanding of the renal vascular architecture and an ability to cool the kidney for an extended ischaemic period make it possible to evacuate completely staghorn calculi or multiple stones from the renal collecting system. Operative radiology of the kidney is most important and careful repair of incised calyceal infundibulae is advocated in the prevention of urinary stasis, which may result from contraction or stenosis of calyceal openings. Such stasis is probably responsible for the recurrence of severe calculus disease.

At the North Carolina Baptist Hospital, U.S.A. experience has been obtained with the use of hypothermia in 320 cases of anatrophic nephrolithotomy.

Sterile ice slush formed in the freezing compartment of a domestic refrigerator in ordinary litre glass containers has been used to maintain the core temperature of the surgically exposed and ischaemic kidney between 15-20°C. The cooling process was continuous throughout the surgical procedure.

The duration of renal ischaemia was shown to be unimportant once the kidney was hypothermic. Estimations of renal function in the immediate post operative and late post operative periods demonstrated that the application of this form of hypothermia to renal surgery was safe, efficient and effective.

During continuous cooling of the kidney with ice slush it was found that core temperatures at two hours showed little variation from those recorded within 15-18 minutes of the commencement of cooling. Accordingly, it would appear to be impossible to overcool a kidney and temperature monitoring throughout the procedure would appear to be unnecessary.

Pre-operative Irradiation combined with Cystectomy in the Management of Bladder Cancer

By Willet F. Whitmore Jr., M.D.

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In a selected group of patients with bladder cancer a pilot study of the efficacy of treatment by pre-operative external irradiation and cystectomy has been undertaken.

Each patient in the series received a total irradiation dose of 4,000 rads. over a four week period with cystectomy carried out between one and three months after irradiation. The results would indicate that this regime is not accompanied by any increase in operative mortality or morbidity. Definite down staging of the tumour as a result of irradiation therapy occurred in not less than 20% of 138 patients.

It was thought that no benefit derived from pre-operative irradiation of those patients with low stage tumours; in this group the results of cystectomy alone, cystectomy with radiation, radiation alone or cystectomy after failure of radiation therapy were similar.

Pre-operative irradiation was of apparent benefit in the management of high stage tumours subjected to cystectomy. In this group cystectomy was worthwhile in the treatment of bladder tumours which had failed to respond to irradiation. No benefit from irradiation therapy was obtained by patients with tumours at a metastatic stage.

Appreciating that the number of patients in the study is small and that the series is uncontrolled the following inferences have been suggested:

(1) In the management of low stage tumours cystectomy may be reserved for those patients who failed to respond to irradiation therapy. Failure to respond to radiation plus cystectomy may be due to delays in treatment or to iatrogenic spread of the tumour.

(2) For high stage tumours the combination of irradiation therapy and cystectomy gives the best survival. The responses to irradiation alone are roughly the same but the failures of irradiation therapy may be salvageable by cystectomy.

(3) Failure to improve the results of cystectomy for metastatic stage tumour is not surprising because the causes of failure to respond are outside the radiation portals.

Certain bias in selection is worthy of special note:

(*a*) Those patients presenting for cystectomy who have failed to respond to irradiation therapy do not include the best results of this treatment (the cures) or the worst results (those who have died).

(*b*) Down staging of the bladder tumour by the pre-operative irradiation therapy makes the results of a pathologically staged series appear to be worse than they really ought to be.

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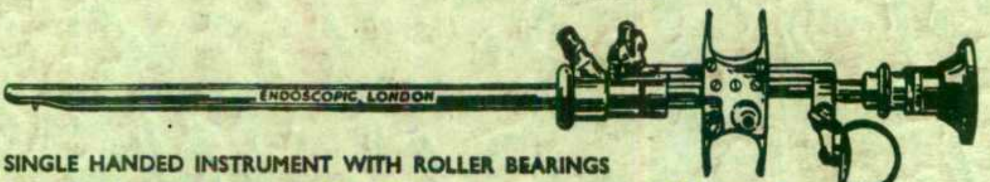

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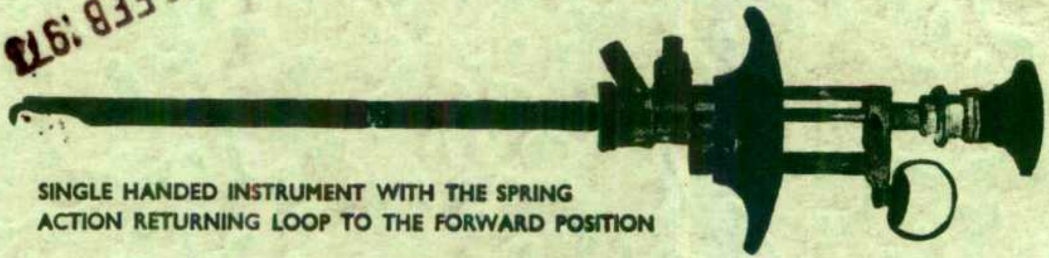

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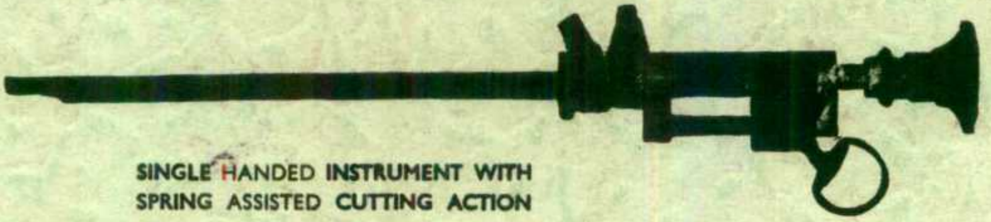

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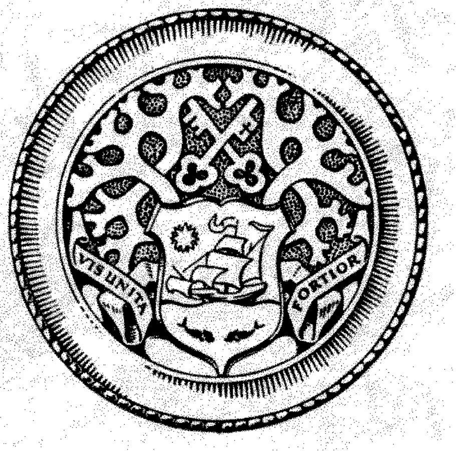

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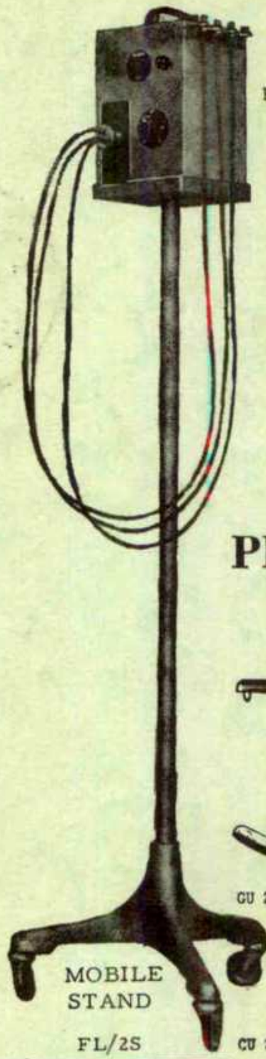

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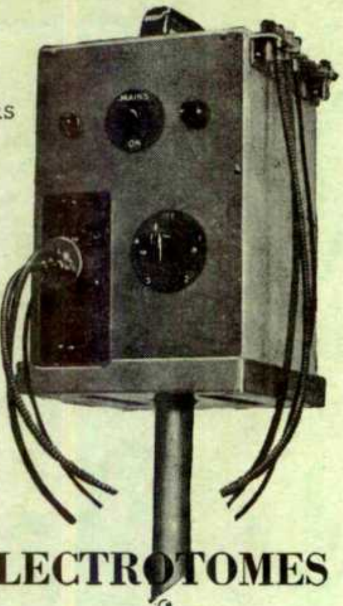

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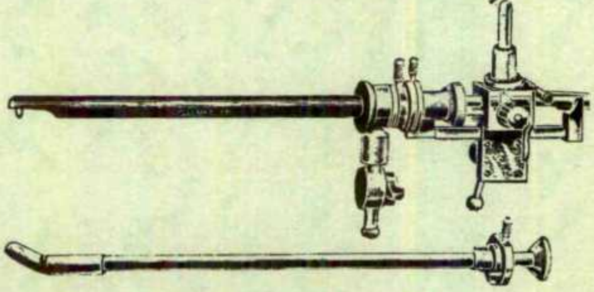

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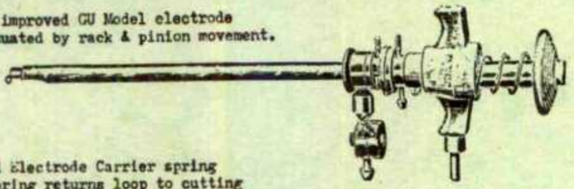

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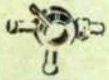

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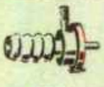

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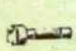

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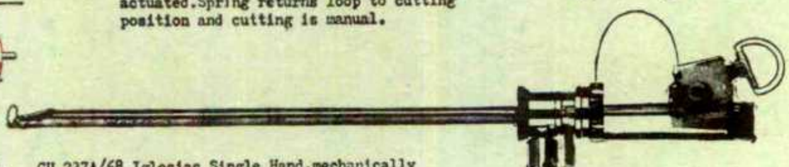

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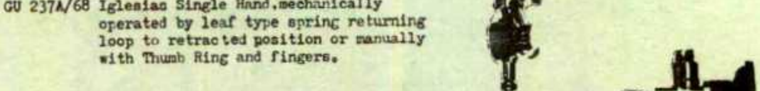

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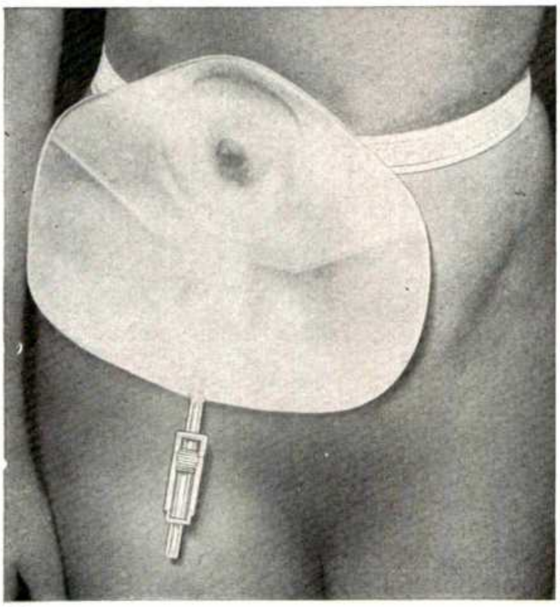

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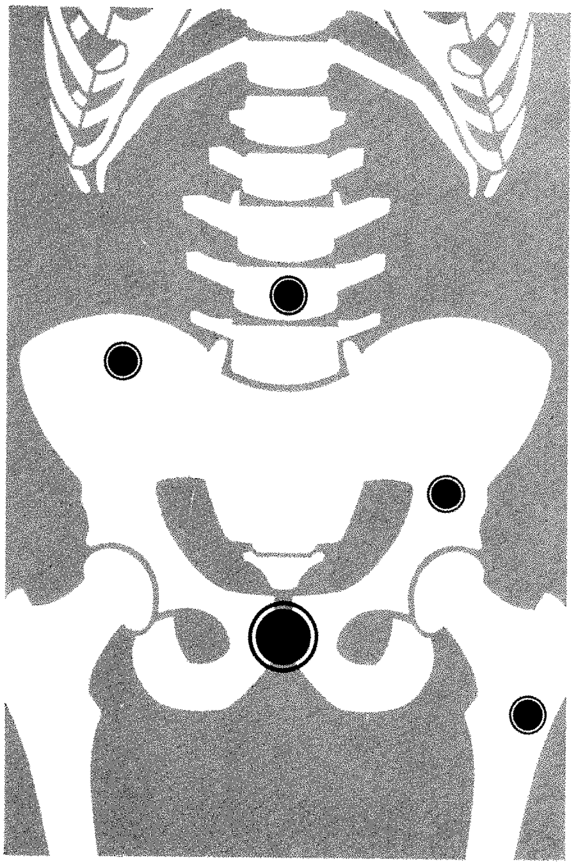

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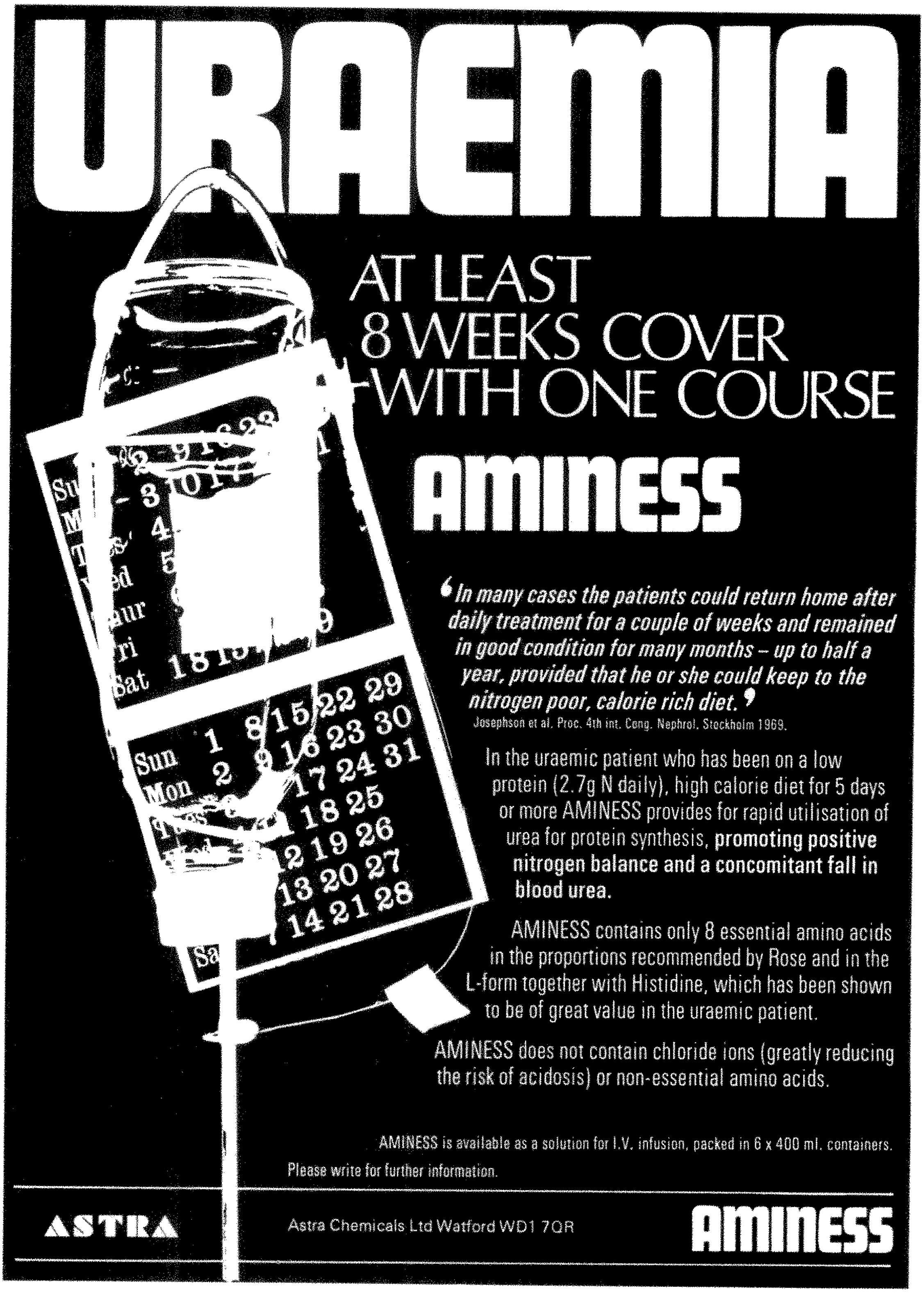

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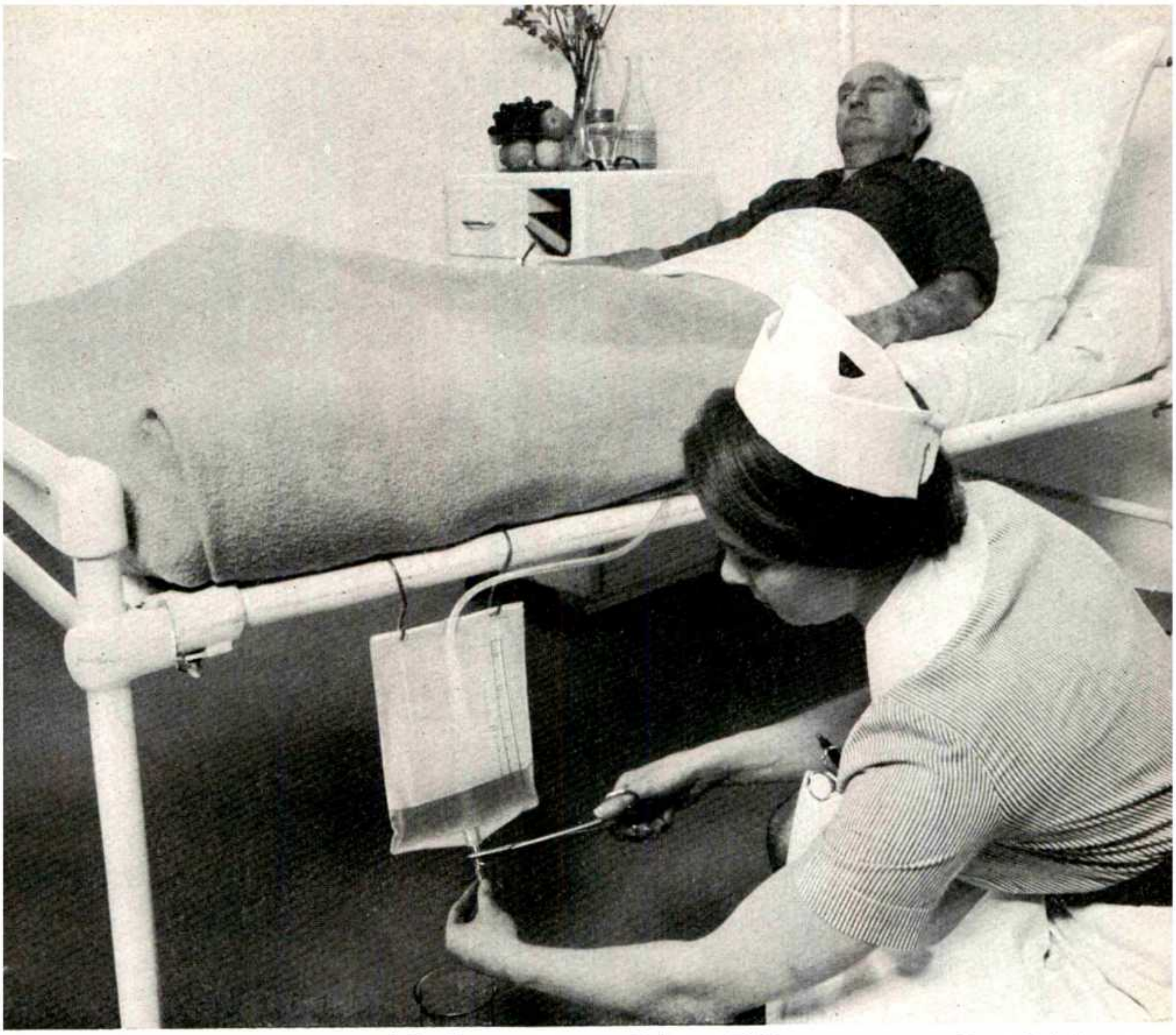

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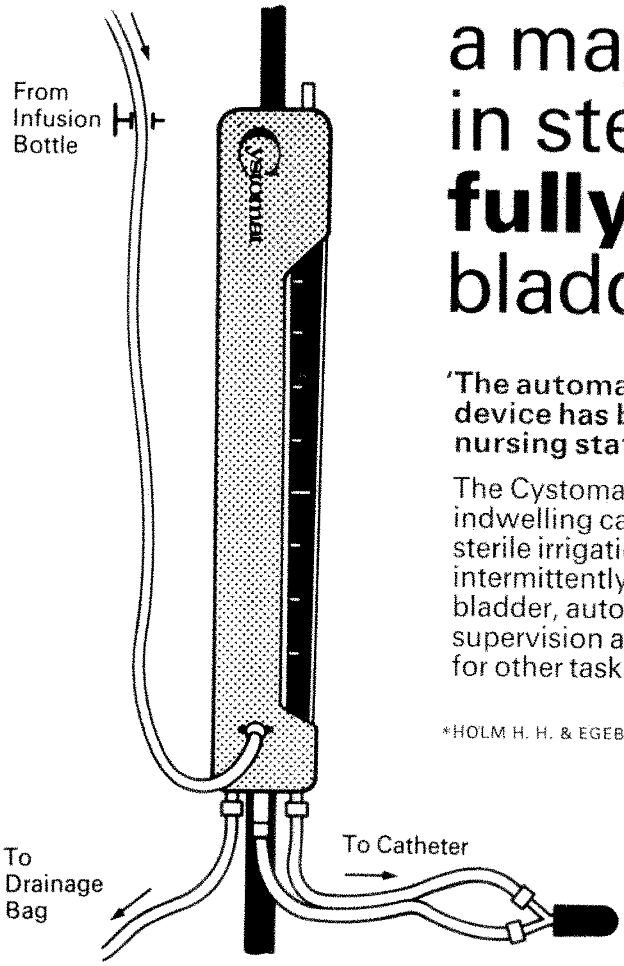

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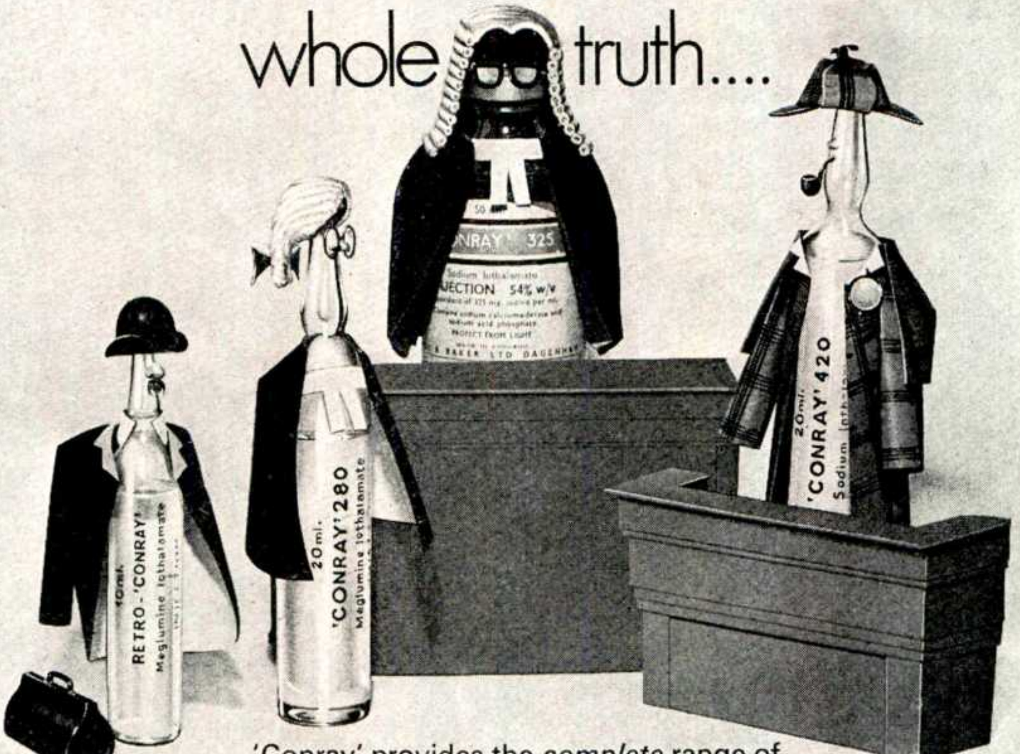

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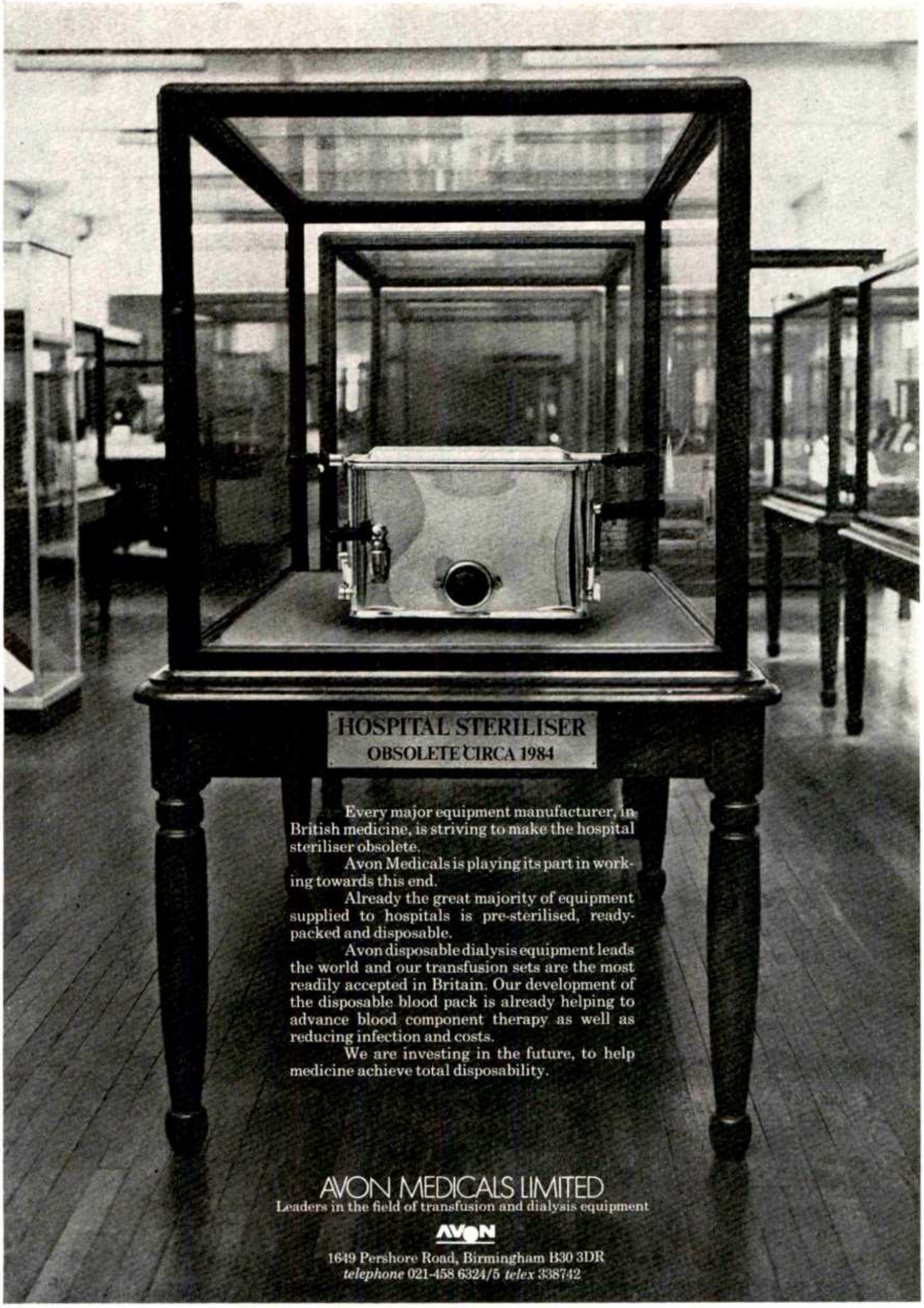

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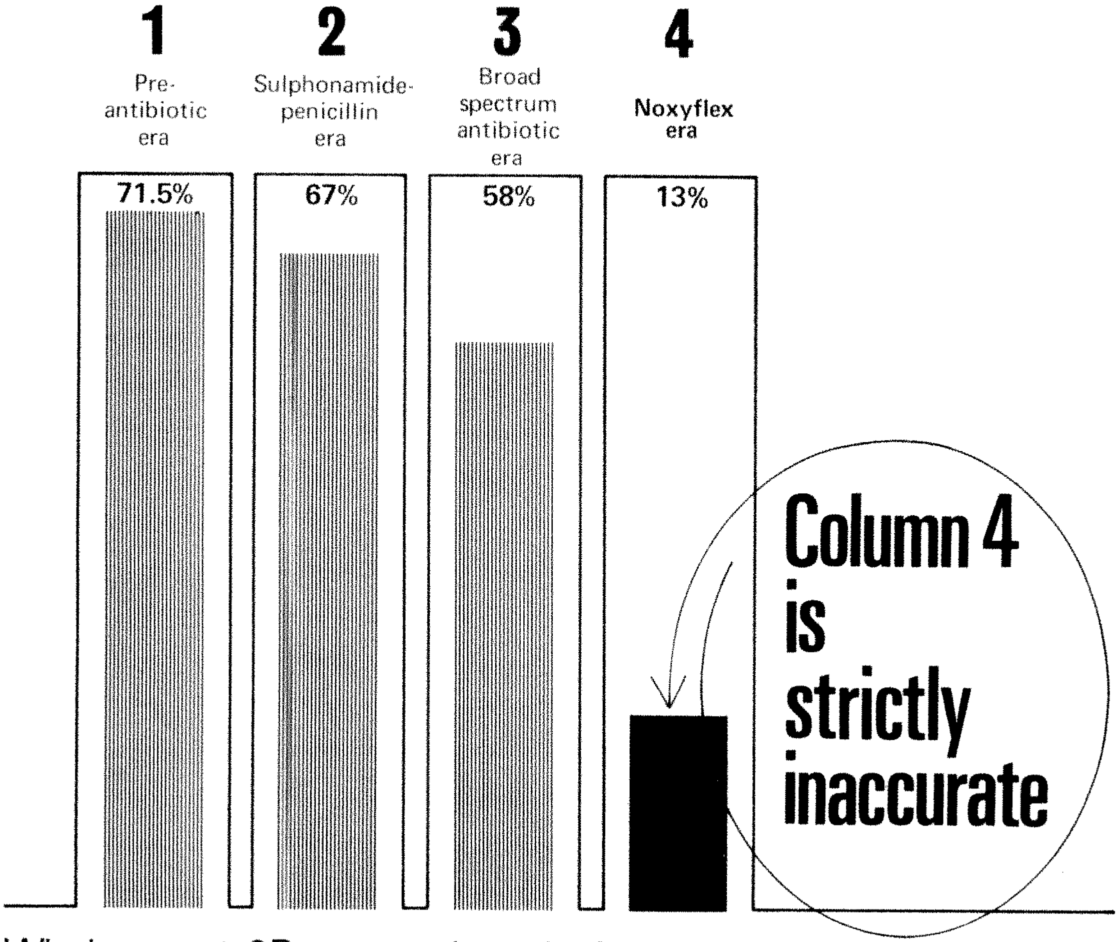

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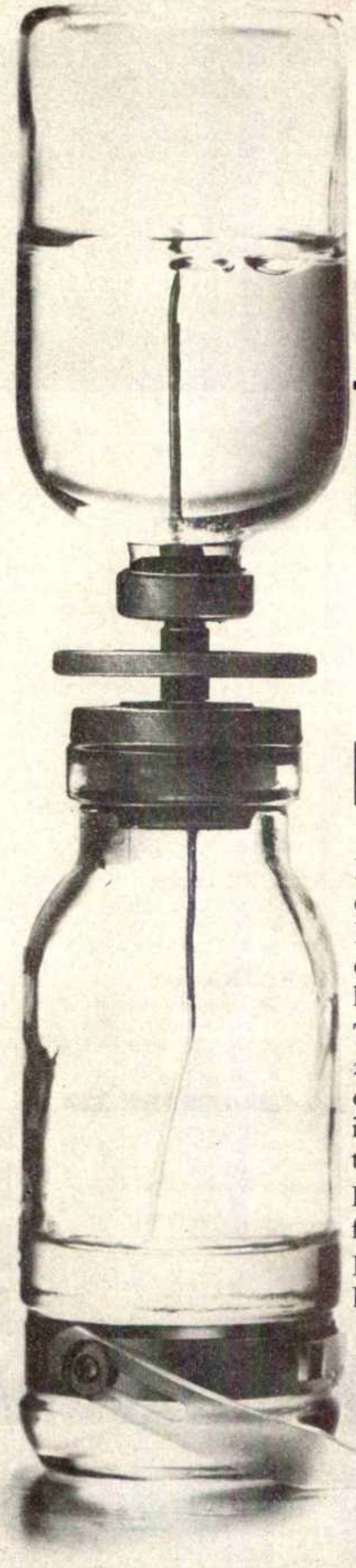

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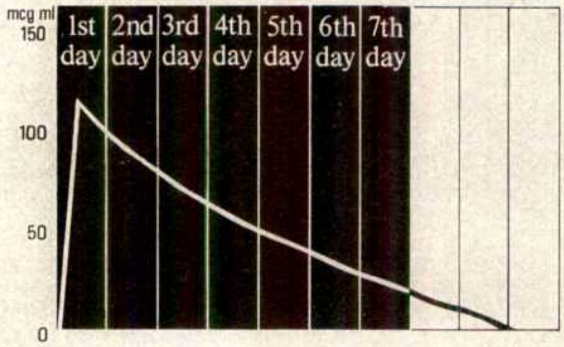

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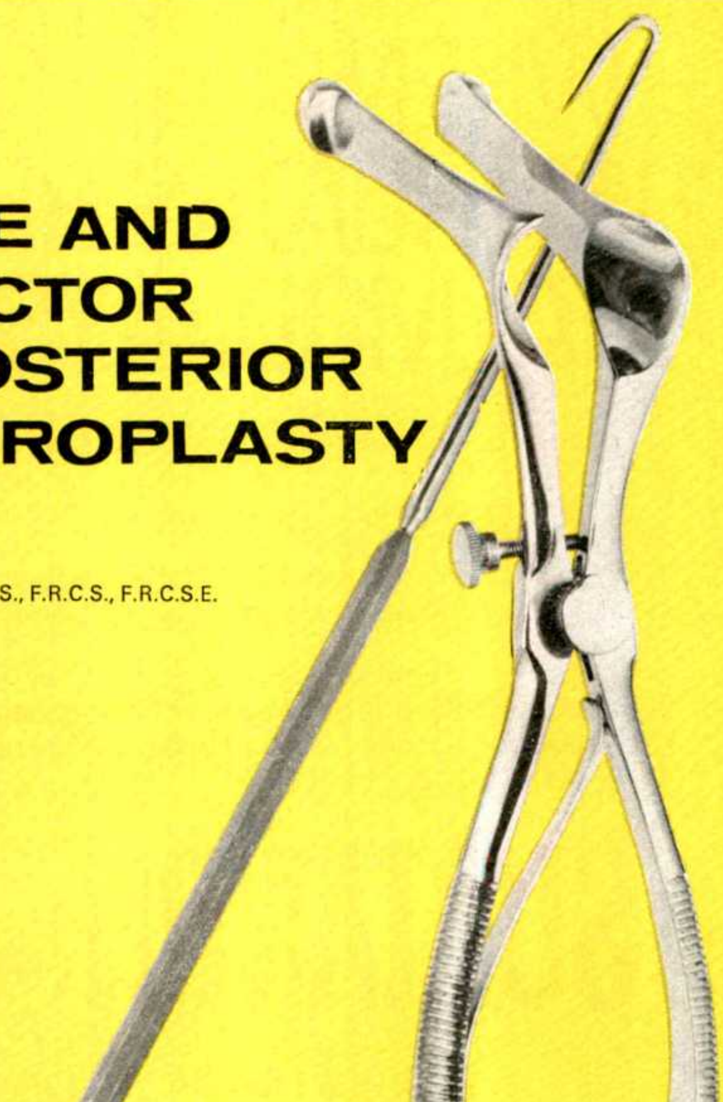

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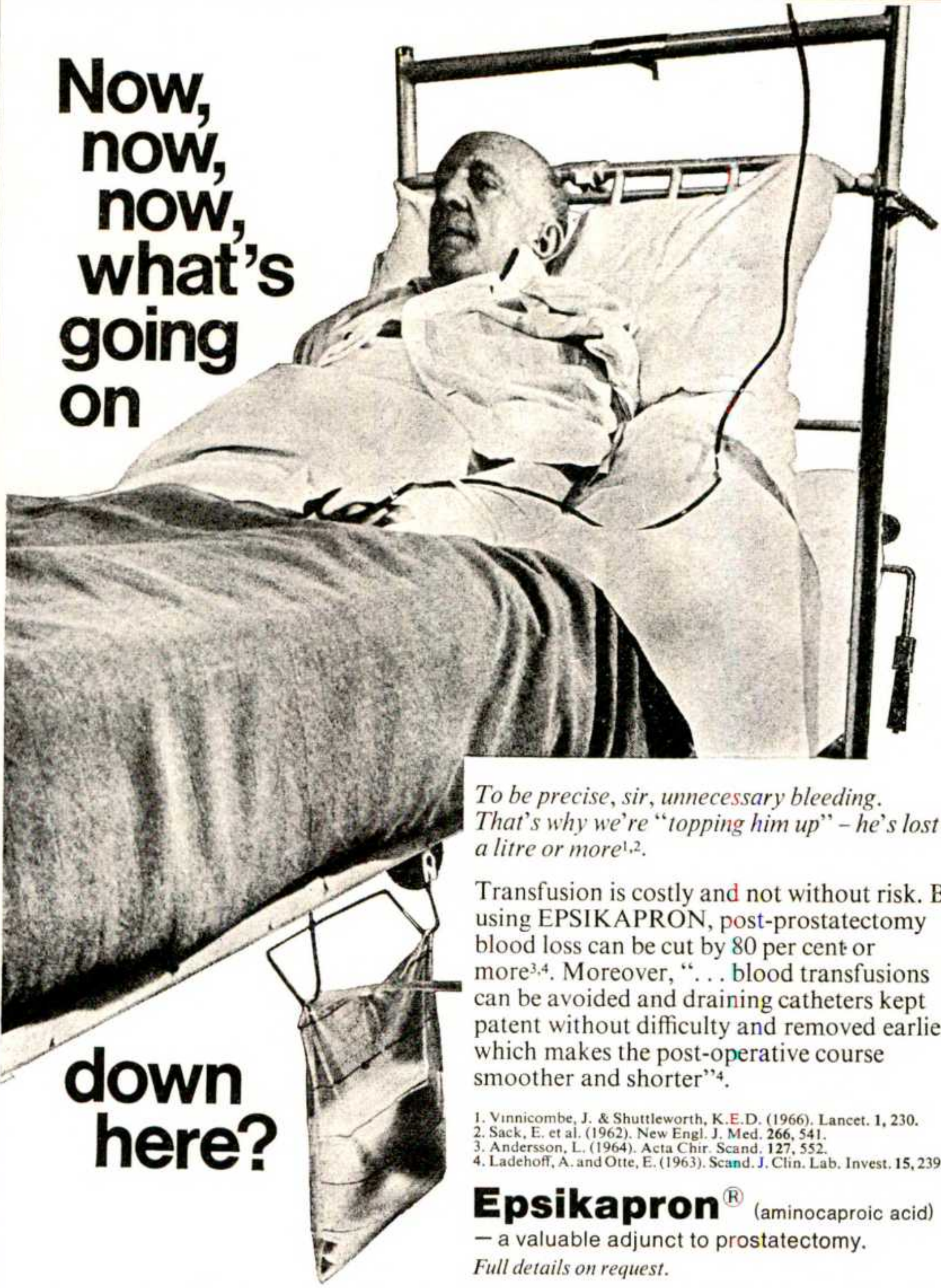

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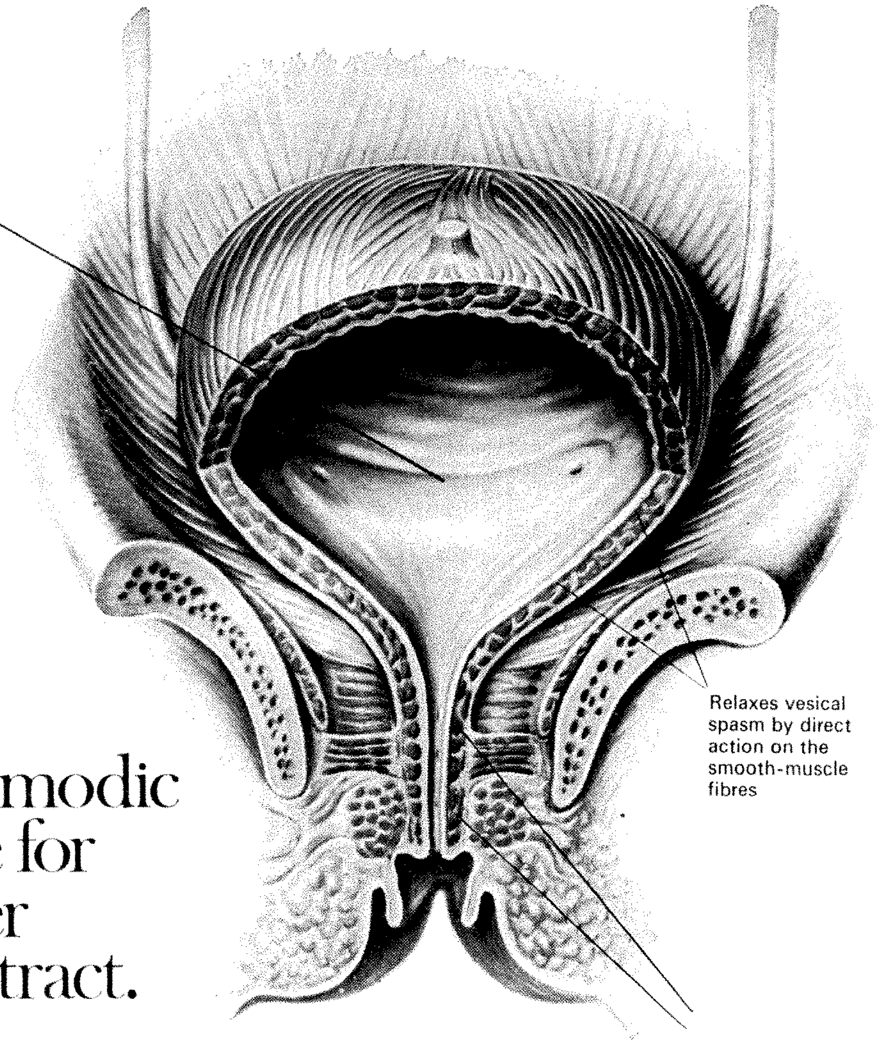

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References:
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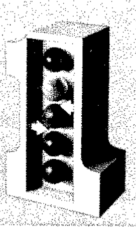

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British Journal of Urology (1972), **44**, 129–132

ANGIOMYOLIPOMA OF THE KIDNEY

Report of Two Cases Presenting as Renal Pelvic Masses

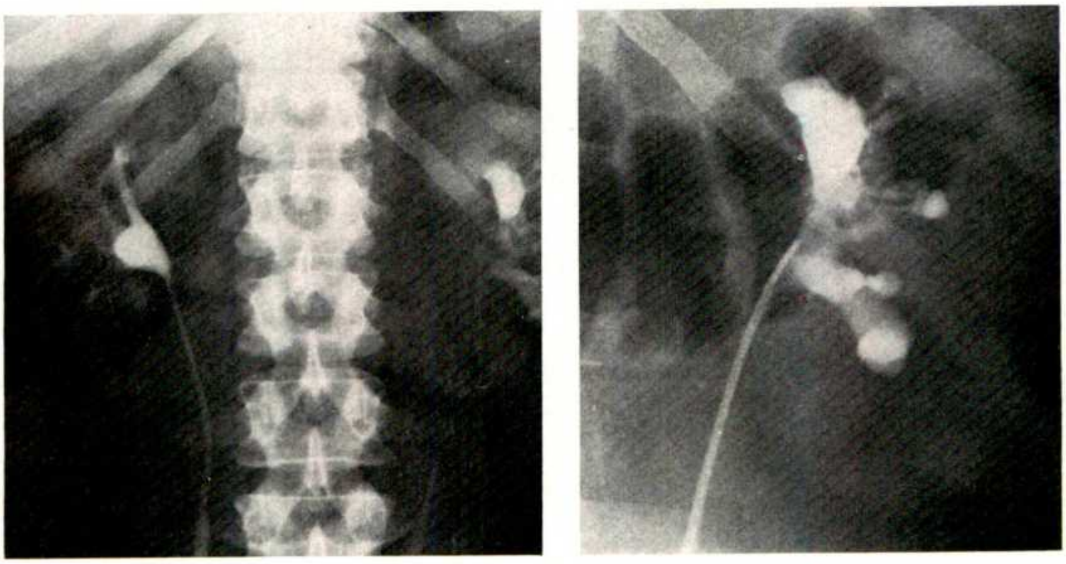
By ALEXANDER S. CASS, F.R.C.S., F.R.C.S.Ed., and GERALD W. IRELAND

Department of Urology, St Paul-Ramsey Hospital, St Paul, and University of Minnesota Medical School, Minneapolis, Minnesota

ANGIOMYOLIPOMA of the kidney usually arises in the renal cortex and expands into the perirenal fat. Presentation of the tumour in the renal pelvis is not common and is reported in 2 cases.

CASE REPORTS

Case 1.—E. C., a 48-year-old male, was admitted on 4 September 1969 with left renal colic. An excretory urogram showed delayed function on the left side with no stone seen. The pain persisted and a subsequent excretory urogram showed a filling defect in the renal pelvis with distortion of the middle calyces of the left kidney and extravasation of dye around the renal pelvis (Fig. 1, A). Similar findings were demonstrated on retrograde pyelograms (Fig. 1, B). Left nephrectomy was performed on 23 September 1969.



A FIG. 1 B

Excretory urogram (A) and retrograde pyelogram (B) showing a filling defect in the renal pelvis with distortion of the middle calyces of the left kidney and extravasation of dye around the renal pelvis.

The pathology report stated, " The lesion extends through the renal pelvis into the renal parenchymal tissue and seems to be demarcated by a connective tissue margin. The well-defined lesion is composed of numerous proliferating vascular channels with some smooth muscle elements and mature as well as fetal fat tissues."

Case 2.—Mrs E. G., a 51-year-old obese female with a long history of hypertension, aortic stenosis and angina-like pain, was investigated in January 1964 for hypertension at another Medical Centre. Bilateral renal cysts were found on excretory urogram and nephrotomograms, but were not felt to be related to the hypertension.

An excretory urogram with nephrotomogram (Fig. 2) in December 1968 at St Paul-Ramsey Hospital revealed an 8·5 cm. mass in the lateral aspect of the lower left kidney and an 8 cm. mass in the upper pole of the right kidney which represented a 2-2·5 cm. increase in diameter of both lesions within 5 years. The right renal pelvis was distorted by a mass which appeared to communicate with the upper pole mass. Renal arteriography was attempted, but the study was unsuccessful.

Transabdominal exploration of both kidneys was performed on 8th April 1969, and a simple renal cyst was found in the left kidney and marsupialised. Solid yellowish tumours were found in the upper pole and in the hilus of the right kidney which was removed. Section of the kidney revealed a dumb-bell tumour extending from the hilus of the kidney through the renal tissue to the expanded upper pole (Fig. 3). The solid mass in the hilus measured 6·0 × 3·0 cm. while the mass in the upper pole measured 9·5 × 6·0 cm. Histology revealed an angiomyolipoma (Fig. 4).

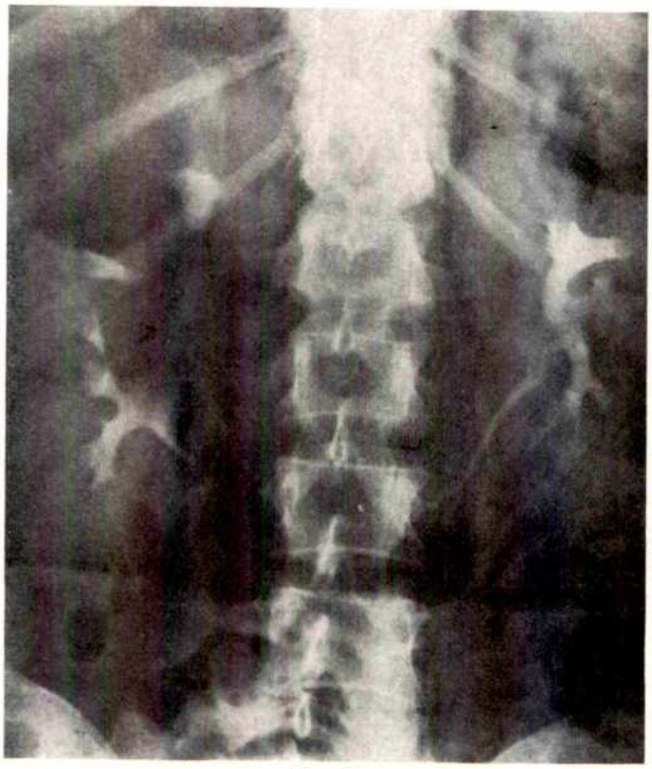


FIG. 2

Excretory urogram revealing bilateral renal masses. The right renal pelvis appears distorted by a mass communicating with the upper pole mass.

DISCUSSION

Renal angiomyolipoma is usually associated with tuberous sclerosis and takes the form of small asymptomatic renal lesions occurring in the young of both sexes. The rarer large symptomatic angiomyolipoma is not associated with tuberous sclerosis and usually occurs in females between the 3rd and 5th decades of life. This benign large tumour is usually unilateral and solitary, but additional smaller foci may be present within the kidney; however, no metastasis from the tumour has been recorded (Price and Mostofi, 1965). The tumour becomes symptomatic because of its size alone or hæmorrhage causing pain. Hæmaturia may also occur.

The tumour consists of fat, smooth muscle and blood vessels and is believed to be hamartomatous rather than neoplastic in origin. The lesion most commonly arises in the renal cortex and growth of the tumour is expansile rather than invasive; the expansion of the tumour is usually from its intrarenal location into the perirenal fat. It is very rare for the tumour to arise

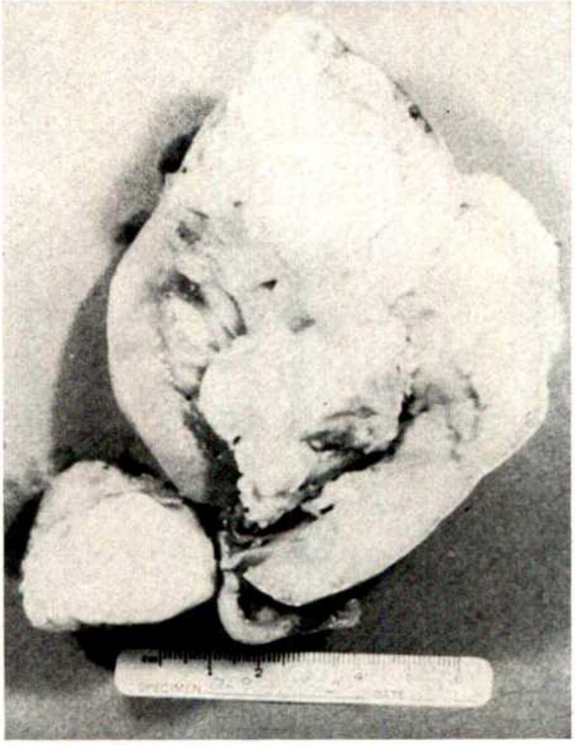


FIG. 3
Section of kidney revealing a dumbbell tumour extending from the hilus of the kidney through the renal tissue to an expanded upper pole.

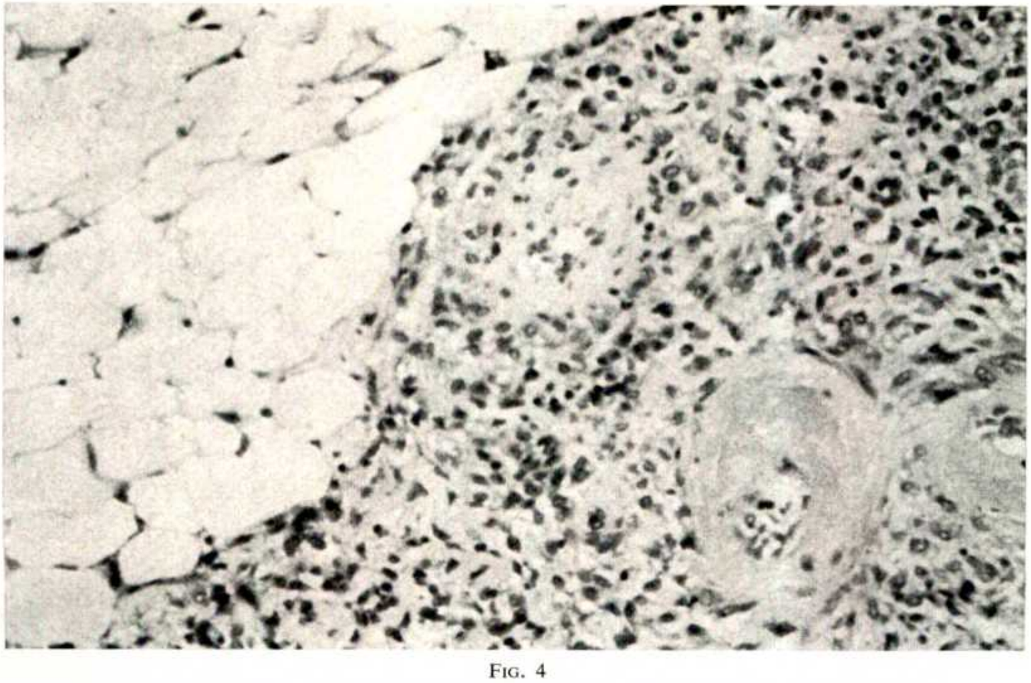


FIG. 4
The tumour is composed of adipose tissue, smooth muscle and blood vessels. H. & E. × 100.

in the renal tissue adjacent to the hilus of the kidney and cause compression of the renal pelvis; seven such cases have been described (Khilnani and Wolf, 1961; Allen and Risk, 1965; Price and Mostofi, 1965; Seabury *et al.*, 1968).

The presence of a single large renal cyst in the opposite kidney is also unusual; 2 cases have been reported in which bilateral polycystic disease of the kidneys was associated with extensive bilateral hamartoma (Inglis, 1954; Klapproth *et al.*, 1959).

SUMMARY

Two cases of angiomyolipoma of the kidney presenting as a mass in the renal pelvis with extension into the adjacent renal tissue of the hilus are recorded.

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British Journal of Urology (1972), **44**, 133–135

AN INTRARENAL FOREIGN BODY

By S. D. CHOWDHURY, F.R.C.S., F.R.C.S.I., F.R.C.S.Ed., and P. M. HIGGINS, M.Ch., F.R.C.S.
North Staffordshire Hospital Centre, Stoke on Trent

FOREIGN bodies in the kidney and renal pelvis are rare. There are three possible routes of entry: (1) external violence, (2) migration from the gastro-intestinal tract, and (3) by retrograde migration via the urethra, bladder and ureter. The last is the least common method. A case of intrarenal foreign body thought to have reached the right kidney by retrograde migration up the right ureter is described.

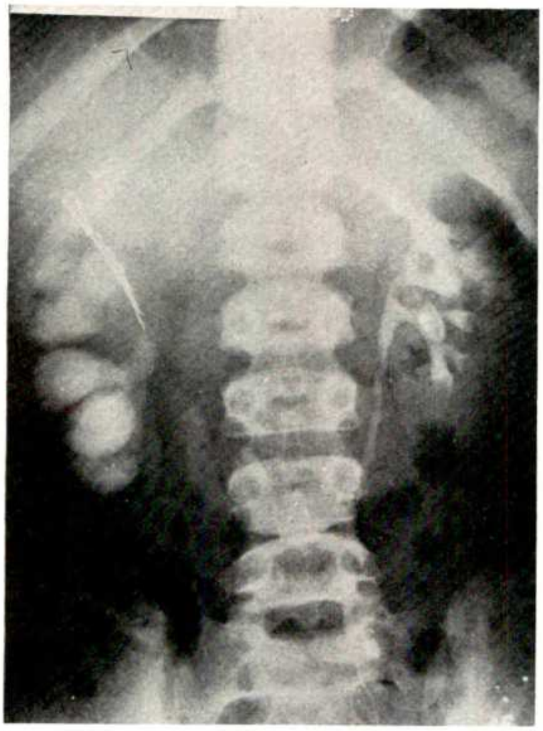

FIG. 1

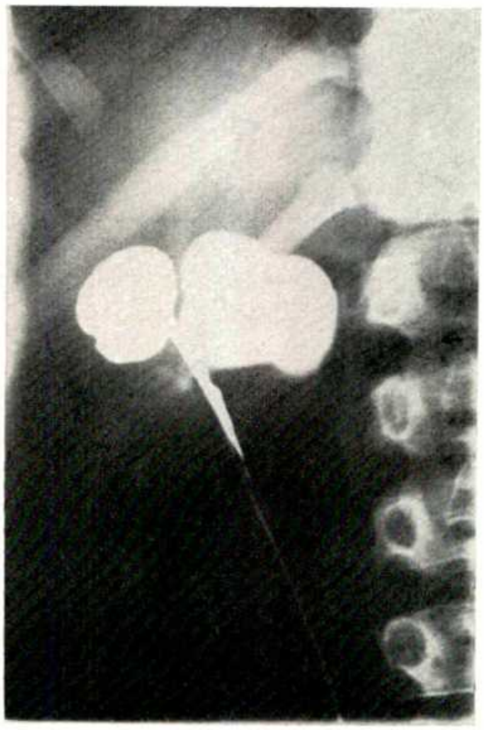

FIG. 2

Fig. 1.—An intravenous pyelogram showing a right-sided hydronephrosis and hydroureter. The hairgrip is thought to be lying in the intestine.

Fig. 2.—A retrograde pyelogram showing the ureteric catheter lying alongside the hairgrip in the right kidney.

Case History.—A 7-year-old girl was seen for the first time in the Urological Clinic on 28th May 1970, having been referred by her general practitioner. During the previous 5 years he had seen her on several occasions with pyrexia, anorexia and abdominal discomfort. He found albumin in her urine in 1965, 1966 and again in 1970. She was referred for further investigation on this last occasion.

When seen in the clinic on 28th May 1970 the only abnormal clinical finding was an enlarged, tender right kidney. Various investigations were carried out.

MSU—Heavy growth of coliform organisms; 5 leucocytes per c.mm.; few red cells. Urea—28 mg./100 ml. Electrolytes—within normal range. Hb.—14 g. per cent. Wbc—8,200, with normal distribution. I.V.P.—" The left side is normal. The right side shows the renal cortex to be thin and scarred. A right sided hydronephrosis and hydroureter is present. A hair grip is noted on the films and is thought to be lying in the intestine " (Fig. 1). Micturating Cystogram—" A normal bladder with no evidence of vesico-ureteric reflux."

On 9th June 1970 her urine again showed a heavy growth of coliform organisms and more than 100 leucocytes per c.mm.

She was seen again on 2nd July 1970 when her urine was still heavily infected with coliform organisms in spite of antibiotic therapy. A further abdominal film showed the hairgrip to be in the same position as previously.

A right retrograde pyelogram was carried out on 16th July 1970. This not only confirmed the previous appearance of the right kidney but also showed that the hairgrip, which was previously thought to be lying in the intestine, was, in fact, in the right kidney lying alongside the ureteric catheter (Fig. 2).

Exploration of the right kidney was undertaken on the 20th July 1970 through a right loin incision. The kidney was found to be enlarged with a thin, irregular upper pole which was adherent to surrounding tissues.

Particular attention was paid to the anterior and medial aspects of the kidney but no adhesions were present between the kidney and the peritoneum. In fact, this plane separated very easily. The hairgrip was removed and an upper pole partial nephrectomy carried out. Histology of the specimen showed chronic inflammatory changes with diffuse infiltration of lymphocytes and plasma cells.

Her post-operative recovery was uneventful and she was allowed home on 4th August 1970. At follow-up on 4th February 1971 her condition was satisfactory, her urine having remained sterile on continuous chemotherapy. An I.V.P. showed some improvement in function.

DISCUSSION

In 1953 Osmond reported 30 cases of renal foreign bodies. In 1968 Baird and Spence reported a further 13 cases. A further case was reported by Nelson and his colleagues in 1953. In the majority of cases the foreign body reached the kidney either by direct violence, for example a bullet lodging in the kidney following a gun-shot wound, or by migration from the gastrointestinal tract. In these latter cases the foreign body (usually a metallic foreign body, *e.g.* a needle) failed to pass the bend of the duodenum or negotiate the splenic flexure. It then perforated the bowel and entered the renal pelvis. However, in 5 cases the foreign body was thought to have reached the kidney by retrograde migration up the ureter. These 5 cases are now considered in some detail.

In 1927 Brattstrom explored the left kidney of a 13-year-old boy having seen blood coming from the left ureteric orifice at cystoscopy. At operation he found 2 grass straws covered with concretions lying in the renal pelvis. He advanced the hypothesis that these straws had been introduced into the bladder by the patient himself during masturbation. Once in the bladder the straws engaged the left ureteric orifice and were then moved upwards to the kidney by reverse peristalses.

In 1929 Blaine described a case in which a broken needle was found in the pelvis of the left kidney of a woman aged 42 years. His explanation for the mode in which the foreign body reached the kidney was similar to that given by Brattstrom.

In 1932 Waring and Drane reported a case of a 37-year-old male patient from whom they removed a seed-bearing grass straw which was present in the right renal pelvis. This patient admitted that he was in the habit of stimulating his urethra with grass or straw and that on one occasion a piece of seed-bearing grass had escaped his grasp and disappeared up his urethra. He never passed the grass in his urine. There seemed to be no other possible explanation than that the grass had ascended the urinary tract and lodged in the renal pelvis.

In 1933 Senger reported a case in which he removed a toothpick from the pelvis of the left kidney of a 40-year-old male patient. He stated that the foreign body could have been introduced into the urethra by the patient himself during masturbation and then ascended the urinary tract to the kidney. He also suggests the possibility that the toothpick could have been introduced during cystoscopy. He states that this latter method is the most likely because at that time many clinics plugged the ends of their ureteric catheters with toothpicks.

In 1953 Nelson and his colleagues described a case in which they removed a " bobby pin " (*i.e.* a hairgrip) from the pelvis of the right kidney of a 4-year-old girl. Their explanation as to how it reached the kidney is similar to that given by the authors of the articles already quoted.

In this present case, a hairgrip was found in the right kidney of a 7-year-old girl. How it reached the kidney is open to question, but it is thought to have reached its destination by retrograde migration up the ureter. As has been stated, foreign bodies can reach the kidney by one of three methods: by external violence; by migration from the gastro-intestinal tract; or by retrograde migration via the urethra, bladder and ureter. External violence can almost certainly be ruled out in this case as there is no history of injury. The possibility of it having reached the kidney from the gastro-intestinal tract is highly unlikely since at operation there were no adhesions between the kidney and the duodenum. Thus, it seems probable that the foreign body reached the kidney by the third route. It is known that the child was in the habit of playing with hairgrips and it is possible that in stimulating her urethra with the blunt end of the hairgrip she inadvertently engaged the right ureteric orifice. Having accepted that the foreign body might reach the lower end of the ureter in this manner it is still far from explaining its presence in the kidney. Clearly, it is not enough to invoke vesico-ureteric reflux as the mechanism by which this occurs. If the ureter were widely distended a foreign body might perhaps be " washed up " to the kidney from the lower end of the ureter, but this could not happen in a ureter of normal calibre. However, when a ureter undergoes peristalsis it shortens in a segmental fashion and it is conceivable that a foreign body in the ureter which was unable to move downwards (the projecting ends of the hairgrip would prevent downward movement) would gradually work its way up the ureter as a result of this sort of peristaltic activity. The mechanism postulated would be similar to that by which a climber ascends a " chimney " in a rock face with the difference that the climber is alternately elongating and shortening himself against the rigid surface whereas in the case of the foreign body, it is the ureter which alternately lengthens and shortens around a rigid object.

Waring and Drane (1932) confirmed, experimentally, the fact that foreign bodies placed in the ureter can move upwards. They operated on a dog and had difficulty in locating the ureteric orifices. They eventually transected one of the ureters and placed a piece of seed-bearing grass in its lower end. Whilst looking for the other ureter, the manipulation caused the foreign body to ascend the ureter by 2 cm.

SUMMARY

A case of intrarenal foreign body in a 7-year-old girl, treated by removal of the foreign body and upper pole partial nephrectomy, is described. The foreign body probably reached the kidney by retrograde migration having been introduced into the bladder, inadvertently engaging the right ureteric orifice and thereafter ascending the ureter to the kidney. It is postulated that the hairgrip was forced up the right ureter to the kidney during peristaltic contractions, the projecting ends of the hairgrip preventing downward movement.

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British Journal of Urology (1972), **44**, 136–142

LYMPHOGRAPHY IN GERMINAL TUMOURS OF THE TESTIS

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A REVIEW of the current status of lymphography in patients with germinal testicular tumours is in order in view of the uncertainty relative to its role in dictating the management of these patients. Toward this end our conclusions drawn from relevant published data are presented and will be supplemented by observations made at our own institution.

Materials and Methods.—(*A*) Reviews of the literature relating to germinal testicular tumours and to lymphography were carried out and data were selected relative to the role of lymphography in the treatment of these neoplasms.

(*B*) From a series of over 600 lymphograms performed at the Royal Victoria Hospital in Montreal, 30 were done on patients presenting with testicular tumours. The method used was basically that of Kinmonth: 8 cc. of Lipiodol[1] were injected into a superficial lymphatic channel isolated from the dorsum of each foot after colouration with Alphazurine 2 g. (Kinmonth *et al.*, 1955). A polaroid film of the knee region was obtained after the introduction of approximately 1 cc. on each side to ensure proper flow through the system, usually paralleling the greater saphenous vein. Immediately after completion of the injection, lymphangiogram films were taken consisting of an A.P. view of the pelvis, an A.P. and a lateral view of the abdomen, and a left posterior oblique view of the thorax to visualise the thoracic duct. Twenty-four hours later, lymphadenogram films were obtained—an A.P. view of the pelvis, A.P., lateral and oblique views of the abdomen, and a P.A. view of the chest. A careful study of both the filling and retention phases of lymphography is necessary since lymphadenogram films may demonstrate normally opacified nodes when the lymphangiogram shows a few channels deviated by abnormal nodes which may be totally replaced by tumour tissue and therefore not opacified.

Results.—(*A*) Pertinent data from the literature are noted under " Discussion ".

(*B*) Table I tabulates the experience with lymphography at our institution. Fourteen of the 30 lymphograms showed either direct evidence of metastases, such as enlarged nodes with filling defects (Fig. 1), or, in one instance, indirect evidence in the form of displaced lymph channels and nodes. Our incidence of positive lymphograms is therefore 46·6 per cent. The intravenous pyelogram was positive in 6 patients, an incidence of 20 per cent. In no case did the intravenous pyelogram allow detection of metastases not demonstrated by lymphography. Conversely, the latter procedure allowed detection of lymph node metastases in nine patients not suspected of having metastatic spread on the intravenous pyelogram (Fig. 2, A and B). Crossover of the medium

TABLE I

Germinal Tumours of the Testis

Number of cases	30
Positive I.V.P.	6
Positive lymphogram	14
Crossover—	
definite	15
questionable	6

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[1] A Guerbet product, Denver Laboratories (Canada) Limited.

FIG. 1

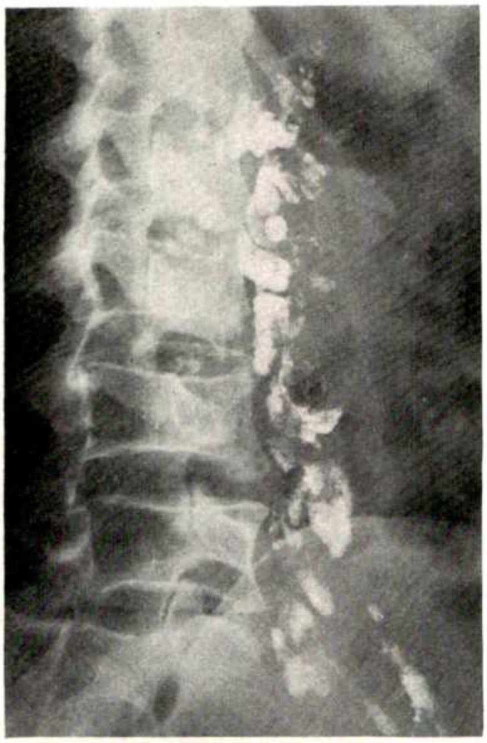
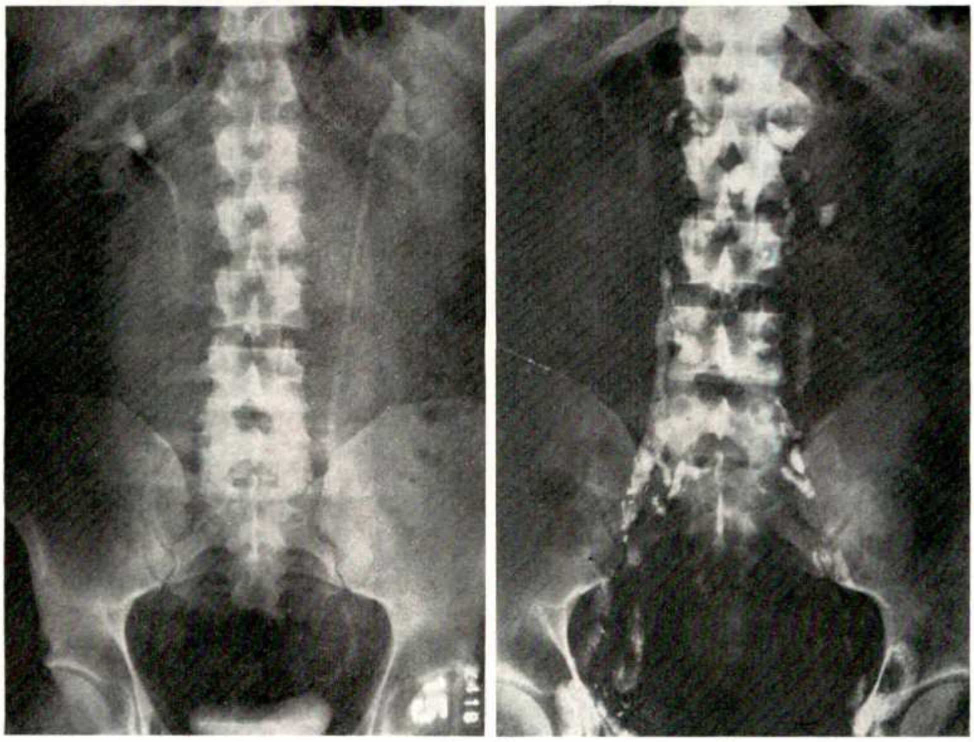


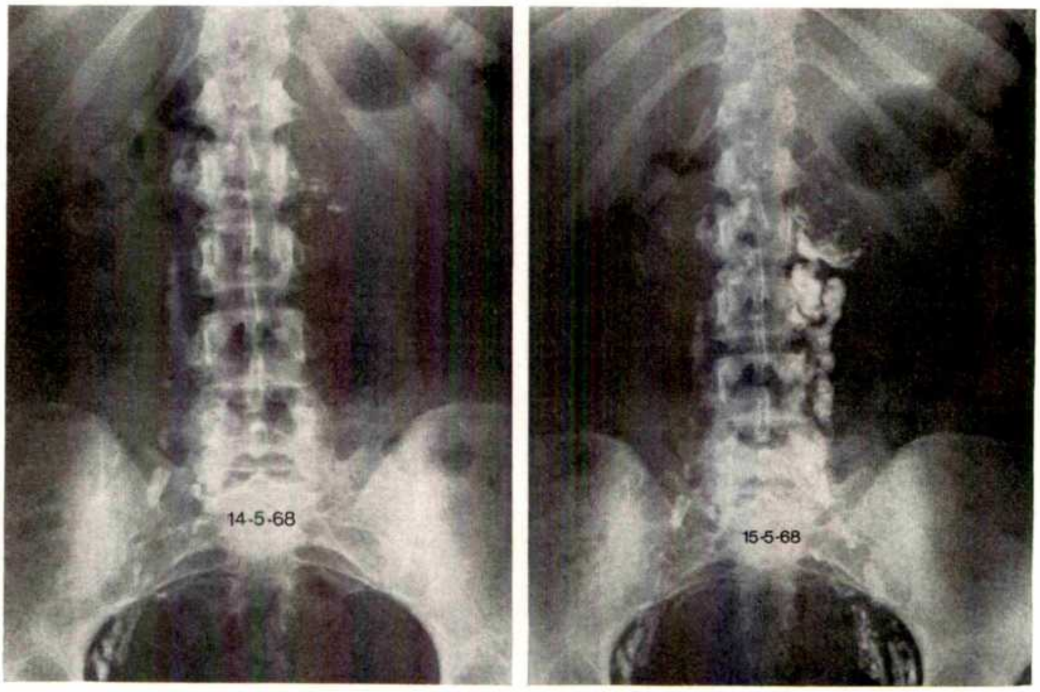
Fig. 1.—Extensive para-aortic metastases from embryonal carcinoma of the left testis.

Fig. 2.—Teratocarcinoma left testis. A, No suspicion of metastasis on I.V.P. B, Metastatic nodes in left para-aortic region on lymphogram.



A FIG. 2 B

in the lymphatic trunks from one side to the other (Fig. 3, A and B) was clearly demonstrated in 15 cases and was questionable in 6.



A FIG. 3 B

A, Right to left cross-over at the level of L2 from injection of a lymphatic of the right foot. B, Injection of the left side on the following day confirming left para-aortic metastases at L2.

DISCUSSION

Prior to the introduction of lymphography, the evaluation of patients with testicular tumours consisted of physical examination, urinary gonadotrophic measurement (or its equivalent), chest roentgenography, intravenous pyelography and, in some instances, inferior venacavography.

A 58 per cent staging error exists between the clinical estimate of the stage of germinal testis tumours, excluding seminoma and choriocarcinoma, as determined by history, physical examination and intravenous pyelogram and the pathologic stage as determined from the study of surgical specimens following lymphadenectomy; that is to say, a patient who has no evidence of disease following orchiectomy, using these diagnostic modalities has a 58 per cent chance of having metastatic tumour in his retroperitoneal lymph nodes (Whitmore, 1970). Fein and Taber (1969) have demonstrated a reduction in staging error to 20 per cent using lymphography.

Apart from direct examination, lymphography is the most reliable and precise method of investigation of the status of the retroperitoneal nodes. Picard and Babinet (1964) have confirmed that although the intravenous pyelogram contributes to the evaluation of patients with testicular tumours, its contribution regarding the demonstration of retroperitoneal metastases remains limited.

The inferior venacavogram is of little value in tumours of the left testis but may be of some help in neoplasms of the right side when nodes infiltrated and enlarged by metastatic tumour indent the contrast-filled inferior vena cava.

Various series have reported very few false positives There are, however, a few false negative lymphograms in cases in which there was *macroscopic* evidence of metastases, partially because foot lymphography does not opacify the primary zone of drainage of the testicle. Most false negative lymphograms occur, however, in cases with only *microscopic* evidence of metastatic disease (Fein and Taber, 1969).

It is important to realise that foot lymphography only allows opacification of the secondary zone of lymphatic drainage of the testis and in only a few instances the primary zone. This primary zone of drainage in the region of the renal pedicles, at the junction of the spermatic vein and the inferior vena cava on the right side and the spermatic vein and the renal vein on the left side can be well visualised by funicular lymphography (Busch and Sayegh, 1963; Book *et al.*, 1965; Chiappa *et al.*, 1966; Wahlqvist *et al.*, 1966). We have not used this particular method, for the following reasons:

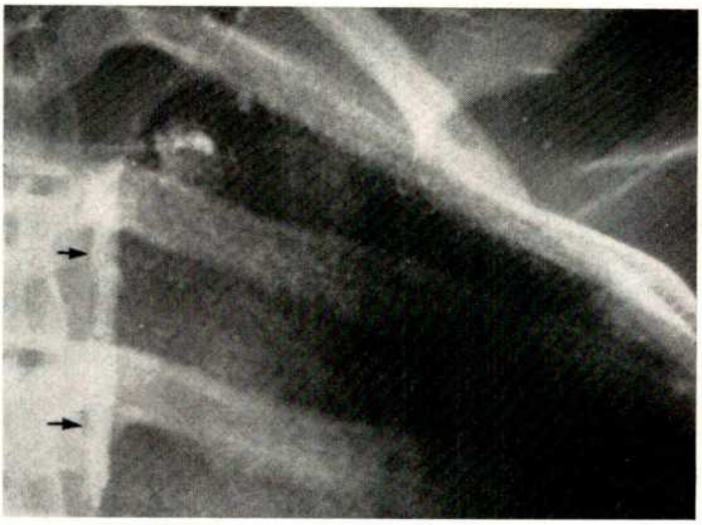


FIG. 4

Terminal portion of thoracic duct (arrows) also showing fine reticulation in lungs from medium in pulmonary arterioles.

1. The injection may not permit adequate filling of the lower para-aortic and common iliac nodes which may be involved by metastases.

2. It has to be performed in the operating room at the time of orchiectomy.

3. As a certain percentage of the oil embolises to the lungs via the thoracic duct and causes a decrease in diffusing capacity (Fig. 4), it theoretically increases the risk of post-operative pulmonary complications (Fraimow *et al.*, 1965).

Our patients are not submitted to general anæsthesia for at least 36 hours after the injection of oil, thus allowing pulmonary function to return to normal pre-operatively

4. It has been postulated that because the injection of oil during lymphography is done under pressure, the flow is not entirely physiological and mechanical distension of the lymph nodes may cause dislodgement of the less cohesive tumour cells, thus enhancing the possibility of metastases (Ujiki *et al.*, 1968). This possibility may be greatest when the transmission from the injection site to the involved nodes is direct as is the case in funicular lymphography. When the injection is done via the foot, however, flow and pressure approximate physiological levels in the external iliac lymphatics, having passed through the first relay nodes in the inguinal region.

Although foot lymphography normally does not opacify the primary zone of drainage of the testis, it has served several purposes in our series:

1. To improve the accuracy of clinical staging.

2. To assess completeness of lymphadenectomy. (A film of the abdomen is done in the operating room before closure of the abdomen to assess the adequacy of resection of the opacified nodes (Fig. 5).)

3. In cases in which a lymphadenectomy was not done, lymphography has been useful in following the response of metastatic nodes to treatment.

4. To evaluate lateral extension of metastatic nodes which will help to determine the site and size of radiation fields.

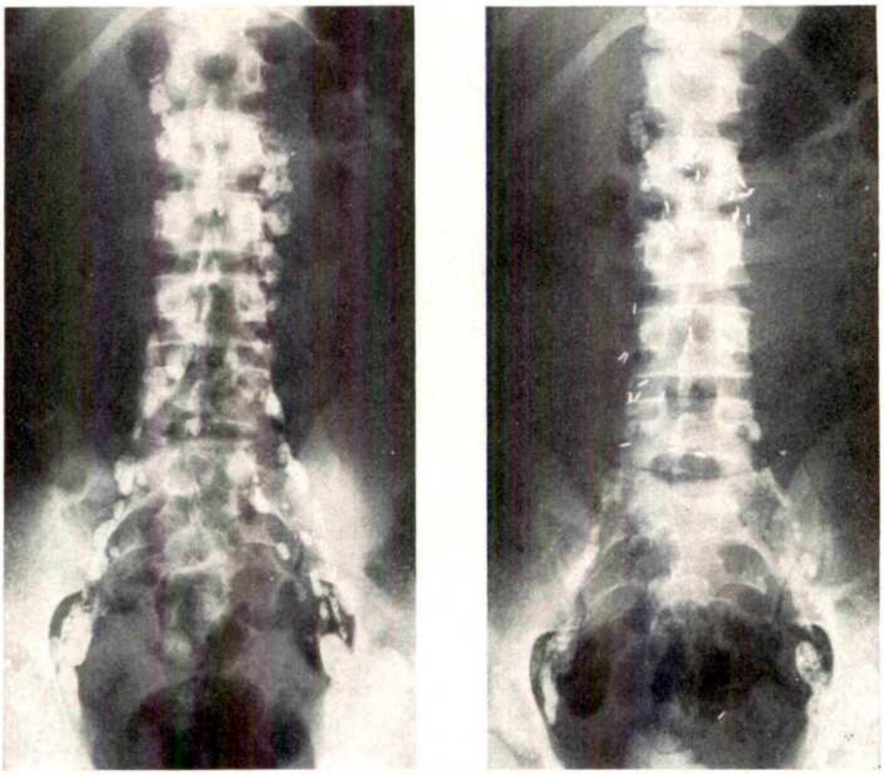


FIG. 5

Left—Metastatic nodes in para-aortic region from teratocarcinoma of the left testis. *Right*—After lymphadenectomy, film of abdomen demonstrating distribution of residual lymph nodes.

5. To demonstrate the course of the thoracic duct. The site of drainage of the thoracic duct is shown on either the lymphangiogram or the lymphadenogram films. In some instances the thoracic duct empties in the right supraclavicular area instead of the left and sometimes bilaterally The knowledge of such variants provides an aid in following the patients with regard to the possible development of supraclavicular metastases (Fig. 6).

Lymphography, in our experience, has demonstrated cross-communication in the retroperitoneal region in the majority of individuals. Funicular lymphography has also demonstrated a degree of cross-over, leading some authors to recommend complete bilateral lymphadenectomy. However, Whitmore (1970) has noted the effectiveness of an extended ipsilateral dissection and that recurrence in the retroperitoneal region following such a procedure is probably unusual. This fact also renders questionable the significance of the frequently demonstrated residual lymphatic tissue in the operative field following lymphadenectomy by a surgeon experienced with this procedure.

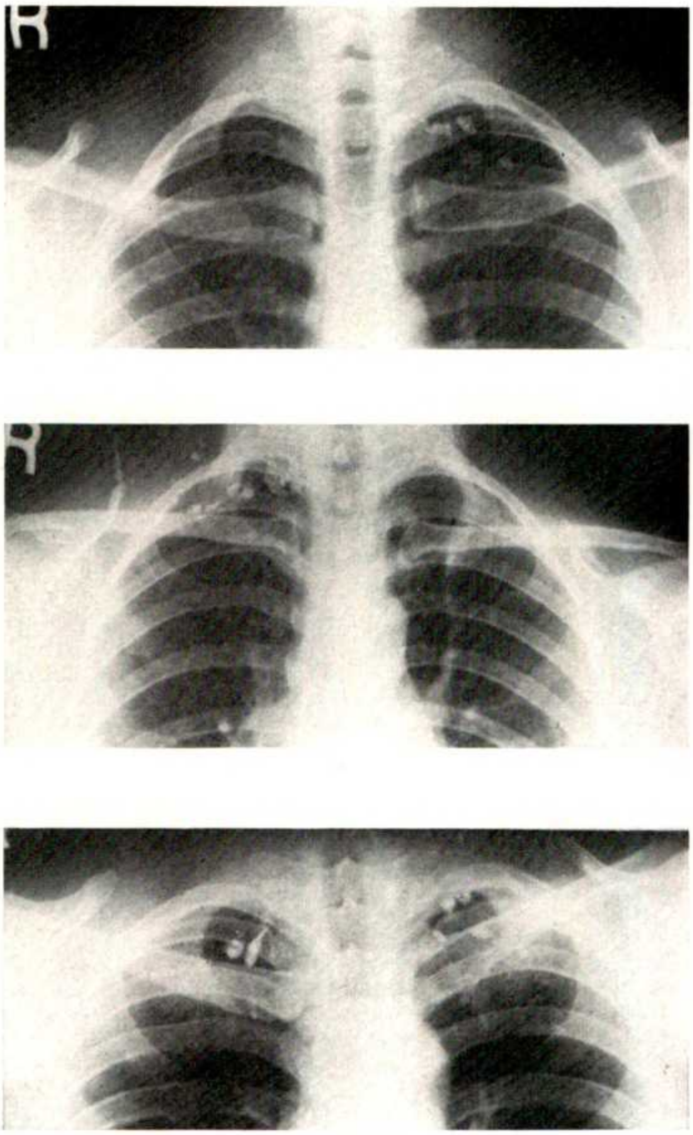


FIG. 6

Various sites of drainage of the thoracic duct. *Top*—Left supraclavicular region. *Middle*—Right supraclavicular region *Bottom*—Both supraclavicular regions.

A further observation of interest regarding the implications of lymphography has been the repeated observance of a reactive œdema and increased stickiness of the retroperitoneal lymph nodes at lymphadenectomy following lymphography (Mount and Whitmore, personal communication).

In their evaluation of the application of lymphangiography, Seitzman and Halaby (1964) comment that it has proven " valuable in predicting the operability of those patients who demonstrate ureteral deviation on the excretory urogram ". We have been unable to support this conclusion since resectability cannot be judged radiographically and even extensive retroperitoneal metastatic tumour deposits can usually be cleanly resected. Nor can their statement be supported by inferring that the presence of radiographically demonstrated extensive retroperitoneal metastasis precludes a favourable prognosis and thus contra-indicates a retroperitoneal lymph node dissection. The combined results of Whitmore and Staubitz's series demonstrate a 66 per cent 5-year survival rate in those patients with *positive* retroperitoneal lymph nodes following orchiectomy and lymphadenectomy *without* adjunctive chemotherapy or irradiation (Whitmore, 1970). Lymphography, therefore, is irrelevant to the choice of modalities used in treating the retroperitoneal lymph nodes.

SUMMARY

Foot lymphography may be used in patients with germinal testicular tumours to improve the accuracy of clinical staging and to delineate the course of the thoracic duct. It also offers parameters for determining the field for retroperitoneal irradiation and for following the response to treatment of the retroperitoneal lymph nodes in those patients not subjected to lymphadenectomy. The implications of lymphography regarding the indication for and extent of retroperitoneal lymph node dissection have been discussed.

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MALIGNANT MELANOMA OF THE PENIS

Report of a Case treated by Surgery and Chemotherapy

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MALIGNANT melanoma of the penis is very rare. Since Joelson's review of the world literature from 1871 (Joelson, 1924) in which he found 8 cases of melanosarcoma (malignant melanoma), 27 cases have now been recorded (Schneiderman, Simon and Levine, 1965; Sirsat and Shrikande, 1965; Patoria and Junnarkar, 1966; Ellis and White, 1968; Fronstin and Hutcheson, 1969). Herein, we are presenting another case of melanoma of the penis, the first in Thailand.

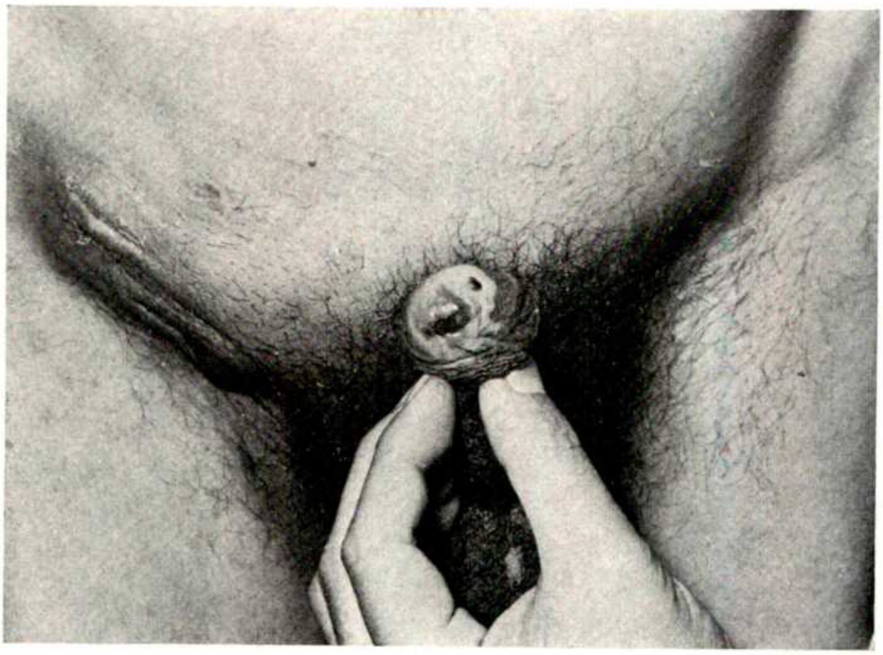

FIG. 1

Macroscopic appearance of the lesion. Note the black area at the external meatus, a black pimple on the dorsum of the penis and discoloured skin in the right groin. The swelling in the left groin is just noticeable.

Case Report.—H.N. 020681, M. K., a 54-year-old Thai, first presented himself to the doctor in March 1969, complaining of an ulcer at the tip of the penis and masses in both groins. One year before any medical attention, a black patch on the penis which had been present for 4 years broke down to form an ulcer. Soon after, a small black pimple appeared near the original lesion. He gradually developed swelling in both groins. There were no urinary symptoms. He had lost nearly 5 kg. in weight.

Clinically, the patient appeared a well-nourished man. All systems were normal. The uncircumcised penis showed an ulcer, 0·2 × 0·1 cm., surrounded by bluish black skin. The lesion involved the right lip and extended on to the dorsal aspect of the external meatus, which was stenosed. A black pimple was found on the dorsum of the glans, 1 cm. away from the main lesion. There were fixed swellings in both groins. The skin overlying the mass in the right groin was thin and bluish (Fig. 1).

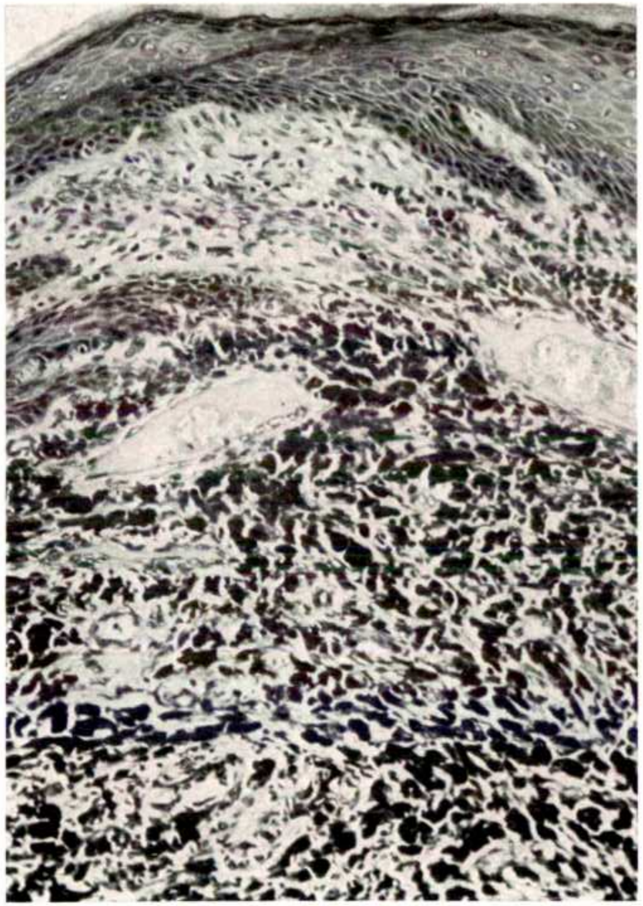

FIG. 2

Photomicrograph of the primary lesion. The covering epidermis shows slight elevation due to a bulky growth of the melanotic tumour. One can see the tumour cells lying close to the basal layer of the epidermis. H. & E. ×100.

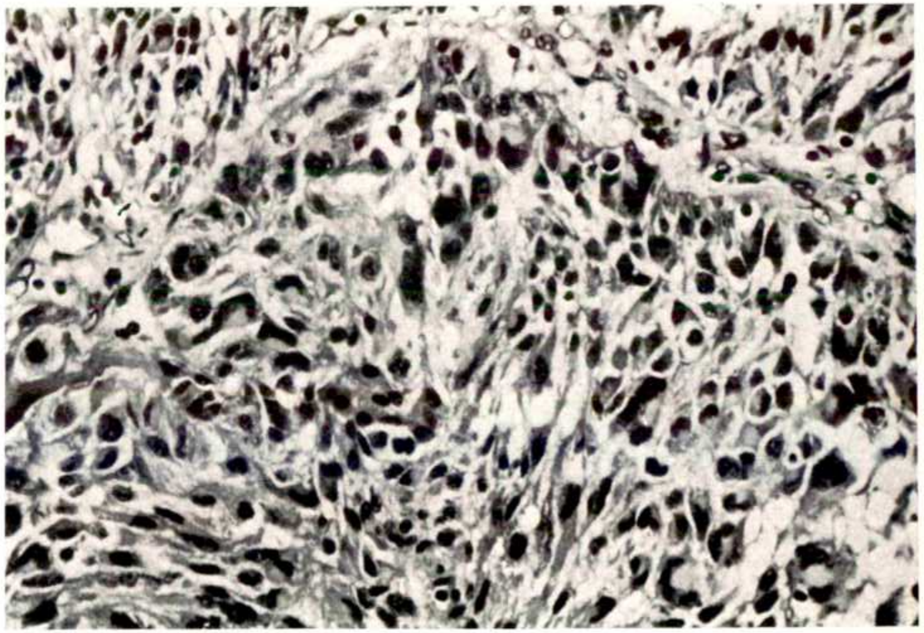

FIG. 3

Photomicrograph representing the deeper portion of the tumour. It shows a mixture of cells. Some are small and fibrillar, some are spindle and some bizarre with both mononucleated and multinucleated giant cells. Melanin pigments can be seen. H. & E. ×400.

Biopsy of the ulcer showed malignant melanoma.

Hæmoglobin—15·2 g., white cell count—9,200 with normal differential, chest X-ray—normal.

On 24th April 1969, most of the phallus, the superficial and deep inguinal lymph glands including the intervening lymphatics were removed in one block employing Young's method (1931). Iliac and obturator nodes were removed after division of the inguinal ligaments. The remaining penile stump was adequate.

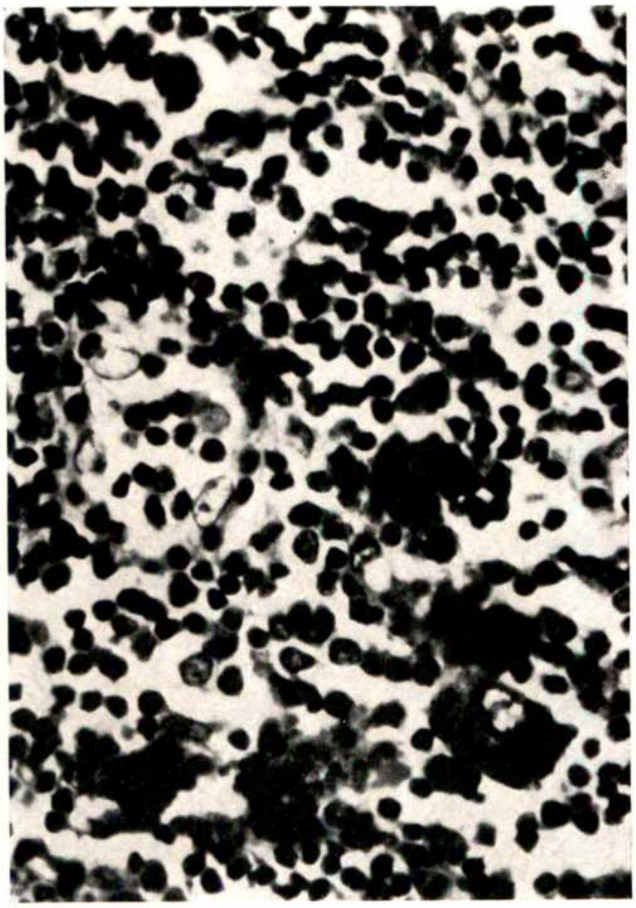

FIG. 4

Photomicrographs of the inguinal lymph nodes. Malignant cells containing melanin pigments can be seen scattered among the lymphocytes. H. &. E. ×400.

The surgical specimen showed no invasion of the corpora. Microscopically, the lesion on the glans penis showed typical malignant melanoma (Figs. 2 and 3) and most of the lymph glands revealed invasion by the tumour (Fig. 4).

His post-operative course was satisfactory. On the 3rd post-operative day, 60 mg. of Alkeran brand of Melphalan or CB 3025 (1 mg./kg.) was administered intravenously. The neutrophil count fell to 4,300 on the 13th post-operative day. On the 3rd week, the neutrophils rose to 7,900. There was no change in the platelets or the hæmoglobin. 4 mg. of oral Alkeran were commenced daily, to be continued for 3 months.

His progress and neutrophil counts while attending the out-patient clinic were satisfactory. At the time of his last visit, 2 years after the operation, he was enjoying good health and had put on nearly 8 kg. in weight. The wounds were well healed. Apart from some swelling in both legs, he showed no signs of metastasis or local recurrences.

SUMMARY

A case of malignant melanoma is reported. The natural behaviour of the disease is mentioned. The treatment is amputation of the penis with incontinuity dissection of the regional lymphatics. Alkeran, a phenylalanine mustard, is employed as an adjunctive in treating the advanced disease.

We wish to thank Mrs Vanna Gojaseni for arranging the manuscript, and Mr Anant for the photographs.

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THE FASCIOMUSCULAR TUBE OF THE SPERMATIC CORD

A Study of its Surgical Anatomy and Relation to Varicocele. A New Concept for the Pathogenesis of Varicocele

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THE spermatic cord is surrounded by a tube of 3 layers: the external spermatic fascia, the cremasteric muscle and fascia, and the internal spermatic fascia. This fasciomuscular tube has not attracted much attention from surgeons as the indications for operations on it are rare. The purpose of this article is to study the surgical anatomy of this tube to understand its function, evaluate its role in the pumping mechanism of the venous return of the spermatic cord, and to find out its possible relation to varicocele.

Material and Methods.—The anatomical, histological and morphological structure of the tube was studied in 20 cadavers of full mature neonatal foetal death. As each side was studied separately, this represented a total of 40 specimens. In 10 cadavers, the tube was dissected, and transverse cut-sections were stained with hæmatoxylin and eosin (H. & E.) and Verhoff Van Gieson (V.V.G.). In the remaining 10 cadavers, the spermatic cord within its tube was dissected free and removed from the level of the external inguinal ring down to the upper pole of the testis. Transverse-cut sections from the upper, middle and lower thirds of the cord were stained with H. & E. and V.V.G.

The morphology of the tube in 10 varicocele patients, aged from 22 to 31 years, was studied during surgical treatment. The varicocele was left-sided in 9 patients and bilateral in 1. Biopsies from the tube were stained with H. & E. and V.V.G.

" Detubation " of the spermatic cord was carried out in 4 adult male mongrel dogs, about 15 kg. each. Animals were examined clinically to ensure absence of varicocele. Detubation was performed on one side, the other was left as a control. A longitudinal incision was made parallel to the spermatic cord as it ran subcutaneously before its disappearance into the inguinal canal. The cord was dissected free, the surrounding fasciomuscular tube was completely excised, and the cutaneous wound was closed. Healing occurred per primam in all animals, and sutures were removed after 7 days. The spermatic cords were re-examined clinically after 4 weeks; one animal was then sacrificed, and both cords were dissected, ligated at both ends, extirpated and fixed in formalin. The same was repeated with the other 3 animals which were sacrificed 6, 8 and 10 weeks post-operatively.

Results.—Microscopical study of the 20 cadavers showed that the external and internal spermatic fasciæ consisted of elastic fibres impregnated with collagen (Fig. 1). The fibres were arranged in longitudinal, transverse and oblique directions giving the fasciæ a textile appearance. The cremasteric muscle bundles were arranged around the cord in 2 groups which were enclosed and connected together with the cremasteric fascia. The latter consisted of elastic fibres intermingled with collagen. Some of the elastic fibres of the cremasteric fascia passed in between the cremasteric muscle bundles (Fig. 2).

A transverse septum arose from the internal spermatic fascia and divided the tube into 2 portions: a large anterior containing the anterior portion of the pampiniform plexus and the testicular artery, and a small posterior containing the posterior part of the pampiniform plexus,

FIG. 1

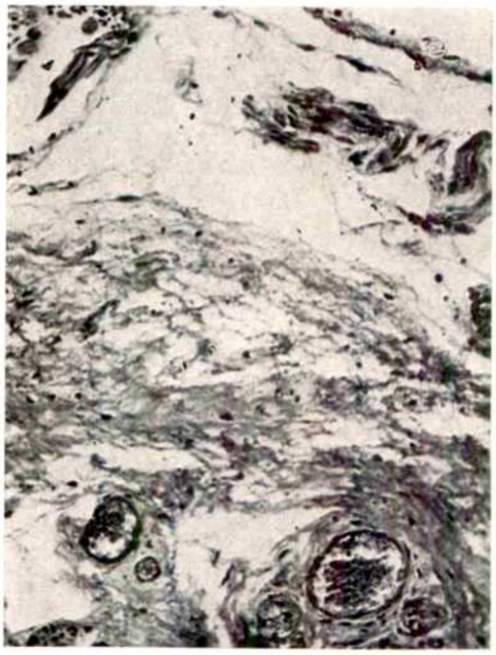
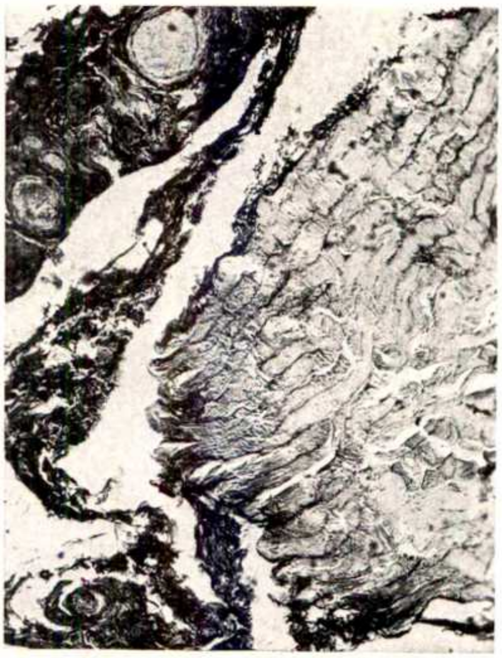


FIG. 2



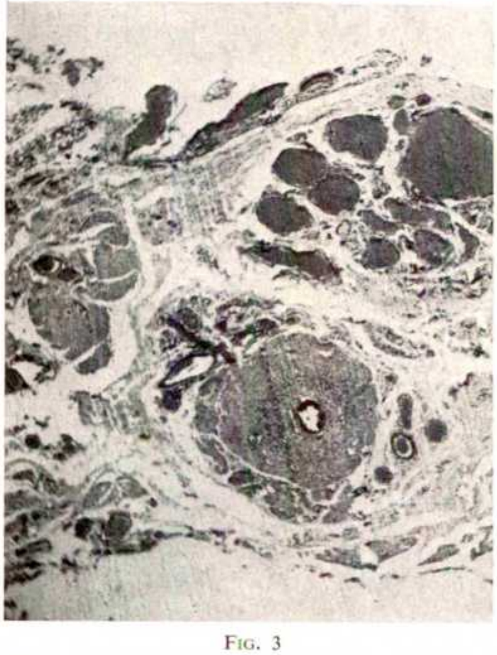


FIG. 3

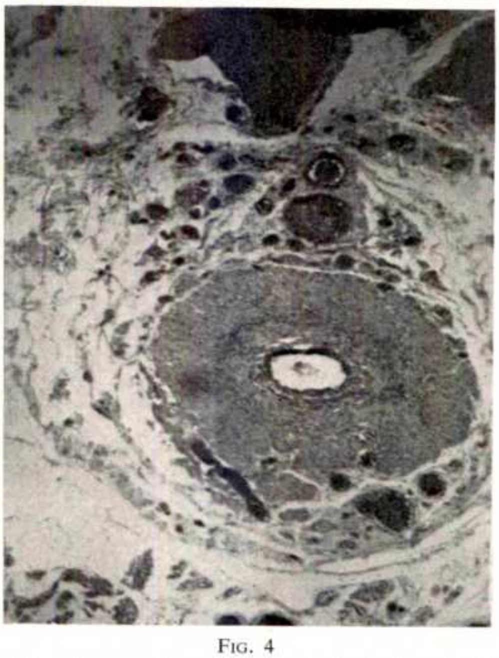


FIG. 4

Fig. 1.—Photomicrograph showing the external and internal spermatic, and cremasteric fasciæ. Each consists of elastic fibres impregnated with collagen. Verhoff Van Gieson. × 84.

Fig. 2.—Photomicrograph showing the cremasteric muscle and fascia. Observe that the elastic fibres pass from the cremasteric fascia in between the cremasteric muscle bundles. (Verhoff Van Gieson. × 378.)

Fig. 3.—Transverse cut-section of the spermatic cord showing the transverse septum which divides the fasciomuscular tube into 2 portions. Hæmatoxylin & eosin. × 28.

Fig. 4.—Photomicrograph showing the posterior cremasteric plexus lying within and around the cremasteric muscle and fascia. Hæmatoxylin & eosin. × 40.

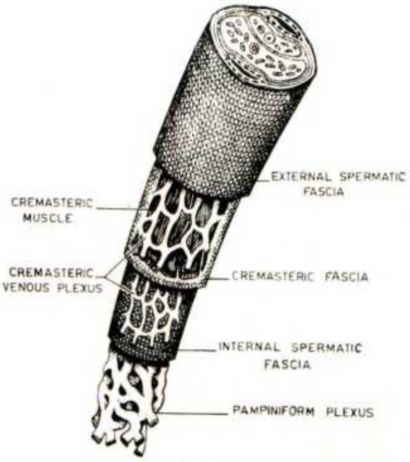

EXTERNAL SPERMATIC FASCIA
CREMASTERIC MUSCLE
CREMASTERIC VENOUS PLEXUS
CREMASTERIC FASCIA
INTERNAL SPERMATIC FASCIA
PAMPINIFORM PLEXUS

FIG. 5

Diagram showing the fasciomuscular tube and the venous plexuses related to it. It demonstrates the textile nature of the fasciæ.

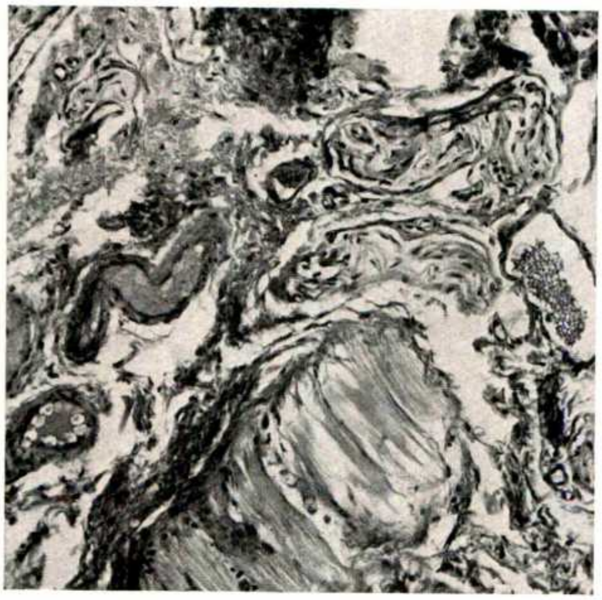


FIG. 6

Photomicrograph showing degenerated cremasteric muscle and dilated cremasteric veins in a patient with varicocele. Hæmatoxylin & eosin. × 120.

the ductus deferens and its artery (Fig. 3). The cremasteric venous plexus consisted of 2 parts: an anterior and a posterior; each was related to part of the cremasteric muscle. The veins lay within and outside the cremasteric muscle and fascia; they were completely outside the internal spermatic fascia (Figs. 4 and 5).

The above findings were demonstrable along the whole extent of the cord.

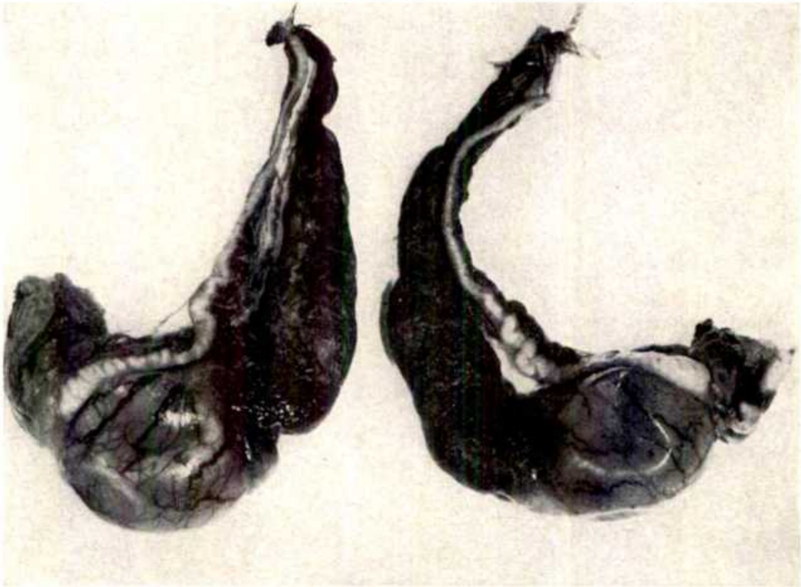


FIG. 7

The " detubated " spermatic cords of 2 dogs showing varicosities. One dog (*right*) was sacrificed 4 weeks after " detubation ", and the other (*left*) at 6 weeks.

Morphological study of the tube in varicocele patients showed that it was flabby and capacious in all the cases. Microscopical study revealed degeneration and atrophy of the cremasteric muscle with remarkable increase of the connective tissue which had replaced the fleshy muscle bundles (Fig. 6). There was diminution or even absence of the elastic fibres of the spermatic and cremasteric fasciæ.

Clinical examination of the dogs 4 weeks post-operatively showed that 3 out of the 4 had enlargement of the pampiniform plexus of the operated side as compared with the control. Pampiniform varicosity was found in the extirpated spermatic cords (Fig. 7). One animal, though sacrificed 10 weeks post-operatively, showed no changes in the pampiniform plexus both clinically and at autopsy.

DISCUSSION

The spermatic and cremasteric fasciæ, being composed of elastic fibres impregnated with collagen, act as an elastic binder to the spermatic cord rather than a passive fibrous sheet. The tube is divided into 2 portions by a transverse elastic septum. The spermatic cord is thus composed of 2 units, each representing a separate pump invested by a layer of elastic fascia (internal spermatic) and supported by a muscular cushion (cremasteric), and the 2 units are wrapped together by an outer common elastic fascia (external spermatic).

This arrangement would seem to help in the mechanism of venous return from the cord. The tube, being derived from the anterior abdominal wall muscles, remains in harmony with changes in them. When these muscles contract leading to an increased intra-abdominal pressure, there is simultaneous cremasteric muscle contraction (being a part of the internal oblique) and pulling on the spermatic fasciæ (being derived from the external oblique and fascia transversalis). This mechanism keeps the elastic stocking surrounding the cord veins right, thus preventing venous reflux from the abdominal veins. Another mechanism is provided by the division of the cord into 2 units which help to increase the pumping mechanism efficiency. The fibres of the spermatic fasciæ, being arranged in a criss-cross pattern, have a textile nature (Fig. 5) which allows the tube to change shape in adaptation to venous pressure changes. The impregnation of the elastic fibres with collagen has an important function. Due to their inelasticity, the collagen fibres limit expressive relaxation of the tube. This mechanism prevents tubal subluxation and flabbiness which may result from venous stagnation during the erect posture.

A New Concept for the Pathogenesis of Varicocele.—The flabbiness of the tube found in varicocele has drawn attention to a possible relation between both conditions. Due to tubal subluxation, the pumping mechanism efficiency is reduced, and the cord veins become less supported and cannot withstand an increased venous pressure during muscular contraction. In addition, the squeezing effect of the elastic fibres is lost due to their atrophy. As a result, the veins become engorged with blood and dilated. This throws an additional load on the already weakened tube and pumping mechanism. A vicious circle which leads to varicocele is thus initiated.

The tube, in addition to its function as a venous pump, suspends the testicle in its normal position in the scrotum. Tubal subluxation leads to lowered testicular position which results in further blood stagnation and varicosity.

This concept for the ætiology of varicocele can be verified experimentaly by cord detubation.

Dilatation is manifested primarily in the cremasteric plexus by transmission through the communicating veins between it and the pampiniform plexus. This is because the cremasteric plexus is less supported as it lies outside the internal spermatic fascia. With further venous reflux and engorgement or with absent communicating veins, pampiniform varicosity occurs.

In the light of this new concept, varicocele is considered to result from a disordered pumping mechanism due to a subluxated fasciomuscular tube.

SUMMARY

The anatomical, histological and morphological structure of the fasciomuscular tube which surrounds the spermatic cord was studied in 20 cadavers of full mature neonatal foetal death and in 10 varicocele patients. The spermatic and cremasteric fasciæ are composed of elastic fibres impregnated with collagen, and act as an elastic stocking to the cord. Together with the cremasteric muscle they form a fasciomuscular pump which may play an important role in the hæmodynamics of the venous return from the cord. Tubal atrophy and subluxation were found in varicocele. Tubal subluxation resulting in inefficiency of fasciomuscular pumping mechanism is discussed as an ætiological factor in varicocele.

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PLICATION OPERATION: A NEW TECHNIQUE FOR THE RADICAL CURE OF VARICOCELE

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Despite the multiplicity of procedures available for varicocele treatment, the results are still unsatisfactory. This is because these operations do not deal with the basic cause of the condition, and may be followed by serious complications. The ideal procedure has yet to be devised.

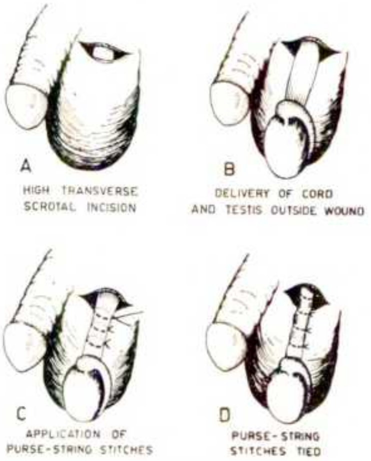
A
HIGH TRANSVERSE SCROTAL INCISION
B
DELIVERY OF CORD AND TESTIS OUTSIDE WOUND
C
APPLICATION OF PURSE-STRING STITCHES
D
PURSE-STRING STITCHES TIED

Fig. 1

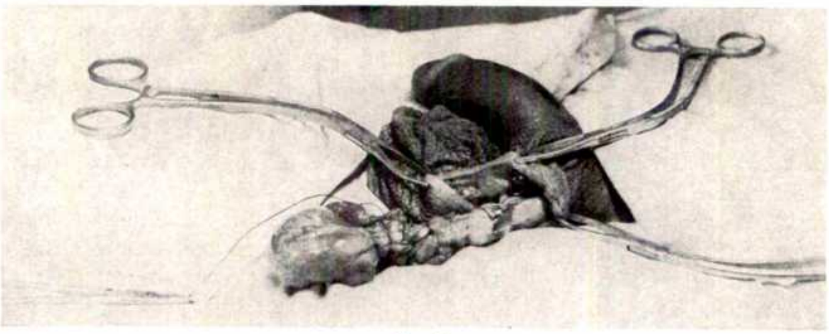

Fig. 2

Fig. 1.—Details of operation.

Fig. 2.—Plication operation for varicocele. The spermatic cord is plicated with multiple purse-string stitches.

Anatomical, histological and morphological studies of the fasciomuscular tube which surrounds the spermatic cord suggest that it plays an important role in the pumping venous mechanism of the cord. In the light of this new concept, an operation has been devised to correct the subluxated tube and the disordered pumping mechanism. The technique has been performed in 52 patients with varicocele. Ages ranged from 25 to 36 years. The varicocele was left-sided in 49 patients and bilateral in 3.

Material and Method.—Through a high transverse scrotal incision, the spermatic cord within its tube and the testis are delivered outside the wound. The tunica vaginalis is everted. The tube is plicated by multiple purse-string stitches, ½ inch apart, starting close to the testis (Figs. 1 and 2). The stitches should include the whole tubal thickness, and, in the lower part of the cord, the everted tunica in addition. The stitches are cautiously tightened to afford support but over-correction must be avoided. If the tube is too capacious, as occurred in 12 cases, a longitudinal strip is excised before the application of the purse-string stitches (Fig. 3). In a further 8 cases, the capacious tube was incised longitudinally and its 2 flaps were overlapped before the purse-string stitches were applied (Fig. 4). The testis and the cord are then replaced into the scrotum, and the wound closed with drainage.

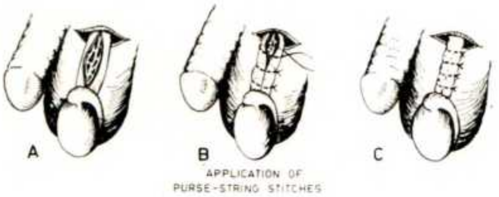

FIG. 3

Excision of longitudinal strip.

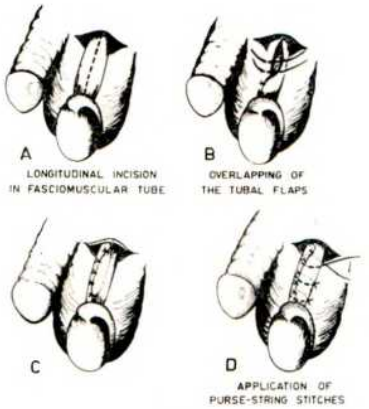
A
LONGITUDINAL INCISION IN FASCIOMUSCULAR TUBE
B
OVERLAPPING OF THE TUBAL FLAPS
C
D
APPLICATION OF PURSE-STRING STITCHES

FIG. 4

Incision and overlapping.

Results.—The convalescent period was smooth in all the cases. Intrascrotal hæmatoma did not occur. Scrotal pain was experienced by some patients in the first few post-operative days. One week after the operation, the testis was at a normal level, and the scrotum was no longer redundant. Of the 52 patients operated on, 38 were followed up for more than 5 years with no recurrence or testicular atrophy.

DISCUSSION

The plication operation aims at correction of tubal subluxation in order to establish an efficient fasciomuscular pump. The improvement which follows the operation may be attributed to:

1. The better support to the cord venous plexuses, preventing their further dilatation and improving the pumping mechanism efficiency.
2. Venous decongestion which is achieved by the support of the purse-string stitches and later by the fibrosis induced by them.

The operation deals with varicosities whether in the pampiniform or the cremasteric plexuses. According to Hanley and Harrison (1962), a varicocele may be a disorder of the cremasteric and not the testicular veins. Dealing with the pampiniform plexus or the testicular veins would thus worsen rather than improve the impaired venous drainage.

The different operations devised for varicocele treatment have always been directed towards the treatment of the mechanical effects of the varicosity rather than the basic causes. In this respect, the plication operation may be regarded as an attempt at correction of a basic factor responsible for varicocele production.

SUMMARY

A new technique for varicocele treatment is described. It consists of plication of the fascio-muscular tube of the spermatic cord, aiming at correction of the tubal subluxation commonly found in varicocele. Fifty-two patients were operated on with encouraging results. The factors to which the results may be attributed are discussed. In contrast to the other commonly practised procedures, the plication operation is an attempt at correction of a basic factor responsible for varicocele initiation.

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ACUTE RENAL FAILURE FOLLOWING ANALGESIC OVERDOSE IN G6PD DEFICIENCY

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THE association between the abuse of analgesics containing phenacetin and chronic interstitial nephritis with renal papillary necrosis is now well established (Spuhler and Zollinger, 1953; Larsen and Moller, 1959; Nordenfelt and Ringertz, 1961; Reynolds and Edmondson, 1963; Dawborn *et al.*, 1966; Prescott, 1966). Less well known is the oxidant effect of phenacetin causing acute hæmolysis in susceptible persons, notably those with red cell glucose-6-phosphate dehydrogenase (G6PD) deficiency (Houston and Barlow, 1959; Gilles and Ikeme, 1960; Harley, 1961; Harley and Robin, 1962; Dodion-Fransen, 1963). The combination of phenacetin intoxication and acute hæmolytic renal failure with subsequent papillary necrosis has not been reported. Finally, chronic ingestion of phenacetin has been shown to cause sideroblastic anæmia in a few patients (Dacie and Mollin, 1966), but this has not been described as a complication of acute analgesic overdosage.

Case Report.—A 33-year-old West-Indian Negro male was admitted to another hospital in June 1969, 3 hours after taking 100 Codeine Compound tablets. As each tablet of Codeine Compound contains 250 mg. of Phenacetin, 250 mg. of Aspirin and 8 mg. of Codeine, a total of 25 g. of Phenacetin, 25 g. of Aspirin and 800 mg. of Codeine was ingested. Five months previously he had taken a small amount of the same type of tablet without any ill effects. He was not admitted to hospital on that occasion. In the past he had had occasional episodes of epigastric pain relieved by antacids,and headaches for which he took various analgesics, reputedly in small quantities. He had had no previous symptoms of loin pain, renal or ureteric colic or hæmaturia. There was no past history of any untoward reactions following drug ingestion by the patient or his family.

On admission he was fully conscious, but depressed. He was neither anæmic (Hb. 90 per cent, 13·3 g. per cent), nor icteric, and there were no abnormal physical findings. His urine was recorded as being " reddish " in colour. The blood urea and serum salicylate levels were not measured at this time. A stomach washout was performed on admission. This was followed by the intravenous infusion of 2½ litres of dextrose-saline over 24 hours combined with a single initial dose of 60 mg. of frusemide, which produced a good diuresis (Fig. 1). He remained well, normotensive and maintained a satisfactory urine output while receiving 3 litres of oral fluids daily. On the 3rd day he started vomiting and became oliguric. There was no response to an infusion of 500 ml. of 10 per cent mannitol. At this time his blood urea was 109 mg./100 ml., his serum was stained deep brownish-red by methæmalbumin and oxyhæmoglobin, and the serum salicylate concentration was 21 mg./100 ml. By the 4th day he was icteric and anuric, the hæmoglobin had fallen to 60 per cent (8·9 g. per cent) and the blood urea had risen to 174 mg./100 ml. Oliguric renal failure due to acute intravascular hæmolysis was diagnosed and he was transferred to the Regional Renal Unit at St Leonard's Hospital 5 days after his initial hospital admission. On examination: fully conscious, B.P. 130/70; P 76/min., regular; good peripheral circulation; all other systems were normal.

The association of phenacetin ingestion and a hæmolytic crisis in a West African suggested that the hæmolysis might be due to the analgesic overdose in a patient with a glucose-6-phosphate dehydrogenase deficiency. At no time had he had circulatory collapse and become hypotensive.

Investigations on Admission.—Hb. 44 per cent (6·5 g. per cent), P.C.V. 16 per cent, reticulocytes 13·6 per cent, platelets 289,000/cu. mm. Blood film showed anisocytosis, some poikilocytosis, a few fragmented cells, marked polychromasia and normoblastæmia. Pappenheimer bodies were noted in the red cells. Staining of the blood film for iron revealed many siderocytes and the normoblasts contained coarse siderotic granules; 16 per cent of the sideroblasts were " ring " sideroblasts. No Heinz bodies were seen. There were no abnormal hæmoglobins present, the direct Coombs test was negative, and no defect in coagulation was detected. G6PD screening test 35 minutes (Normal 30-55 minutes). Blood urea 270 mg./100 ml., potassium 4·6 m.Eq./l., serum bilirubin 0·8 mg./ 100 ml. Urine—dark brown with 15 RBC's/H.P.F., 10 WBC's/H.P.F. and some granular casts.

Progress.—Peritoneal dialysis was started immediately and was continued for 12 days. Within 4 days the siderocytes and sideroblasts seen on admission had disappeared from the peripheral blood. He was given 2 units of blood during the period of peritoneal dialysis. From the 16th day his urine ouput began to increase steadily

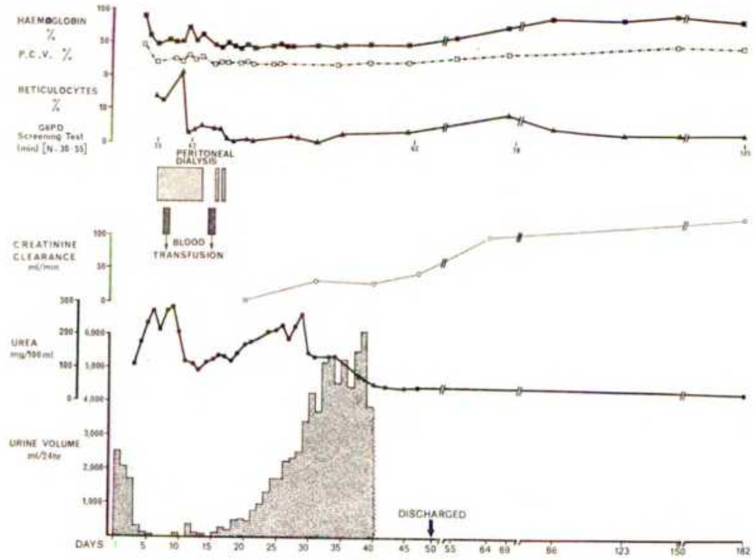

FIG. 1
Clinical course.

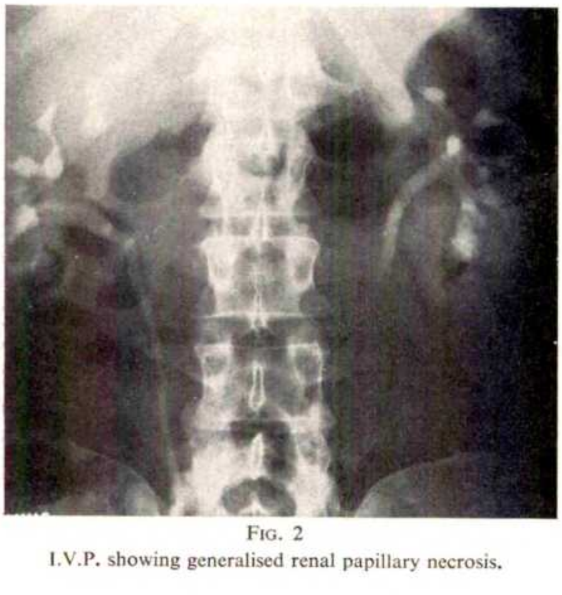

FIG. 2
I.V.P. showing generalised renal papillary necrosis.

and he entered into the classical diuretic phase of acute tubular necrosis, requiring large volumes of fluid and potassium supplements. The blood urea fell and creatinine clearance improved. The hæmoglobin level was very slow to rise.

On discharge creatinine clearance was 76 ml./min., blood urea 45 mg./100 ml. and hæmoglobin 49 per cent (7·4 g. per cent). By the middle of November the hæmoglobin had risen to 86 per cent.

Other Investigations.—An I.V.P. done on the 11th day showed a definite nephrogram of the left kidney at 20 hours. The right kidney was less well shown, but both were normal in size and shape, and there was no evidence of obstruction. A second I.V.P. done in December 1969, 6 months after the episode of acute renal failure, showed the appearance of widespread papillary necrosis (Fig. 2).

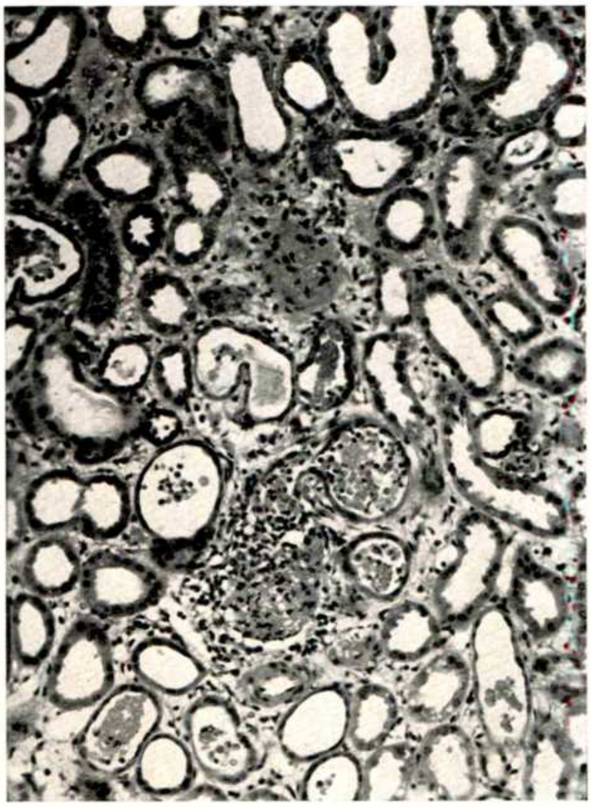

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FIG. 3

Renal biopsy (H. & E. × 150) showing acute tubular necrosis with early tubular regeneration.

Open renal biopsy on the 14th day showed widespread tubular damage and the presence of hæmoglobin casts with some regeneration of the tubular epithelium. There was no evidence of chronic interstitial nephritis (Fig. 3). Staining for iron showed massive deposition of ferric iron in both the normal and disrupted tubular lining cells.

Bone marrow aspiration 5 weeks after admission revealed normoblastic erythroid hyperplasia. Staining for iron showed normal iron stores, and many sideroblasts containing fine siderotic granules. No " ring " sideroblasts were seen. There was no evidence of toxic depression of the marrow, the findings being more suggestive of a response to continued hæmolysis or blood loss.

Fæcal occult blood tests were initially positive and a barium meal showed a deformed duodenal cap indicative of chronic ulceration. Glucose tolerance test showed a normal curve.

The methæmoglobin reduction time was used as a screening test for G6PD deficiency and was initially 35 minutes (N = 30-55 minutes). Subsequent retesting showed an increase in the reduction time (Fig. 1). When it was 78 minutes the G6PD level was estimated directly using a method based on that of Glock and McLean (1953) and was found to be 0·06 μ moles N.A.D.P. reduced/min./ml. packed RBC at 25°C. (Normal = 0·24-0·48 μ moles, Control = 0·42 μ moles).

Comment.—This case illustrates certain previously unreported renal and hæmatological consequences of analgesic overdosage.

A severe hæmolytic crisis occurred as evidenced by the fall in hæmoglobin from 90 per cent to 44 per cent (13·3 to 6·5 g. per cent); the high reticulocyte count; the presence of methæmalbumin and the hæmoglobin casts and iron deposition later found on renal biopsy. It seems probable that the intravascular hæmolysis and hæmoglobinuria were the predominant factors in the ætiology of the acute renal failure and were due to the oxidant effect of phenacetin on the G6PD-deficient red cells. In most normal subjects only a mild hæmolysis occurs with large doses of phenacetin. In the presence of G6PD deficiency, hæmolysis occurs much more readily. In a few cases a genetic defect of de-ethylation in the liver has led to hæmolytic crises after therapeutic doses of phenacetin (Shahidi, 1968) and, exceptionally, phenacetin in small doses may precipitate fulminating hæmolysis by an immune mechanism (MacGibbon *et al.*, 1960).

Acute renal failure following intravascular hæmolysis is well recognised. While the pathogenesis of this event is not clear, a combination of renal ischæmia, hypotension, tubular obstruction and direct nephrotoxicity of free circulating hæmoglobin has been invoked. The degree of renal dysfunction may relate to the magnitude of the hæmolysis.

This patient had severe hæmolysis and presumably considerable methæmalbuminuria. If tubular blockage by hæmoglobin is of importance in the genesis of the acute renal failure, it is of interest to note that despite a good initial water diuresis acute renal shut-down occurred. It could be suggested that a maintained *osmotic* diuresis might have prevented the renal failure. In this context it is important to note the 3-day delay between the ingestion of the drug and the development of manifest hæmolysis. It should be noted that by the 3rd day after the initial ingestion his serum salicylate was still raised at 21 mg./100 ml. Thus the delay in the acute hæmolysis was probably due to delay in absorption of the drug from the gastro-intestinal tract. The experience gained from this case suggests that, following the ingestion of phenacetin containing analgesics, prophylactic, osmotic diuresis may have to be maintained for at least 3 to 4 days if it is to be effective in preventing the complications of hæmolysis.

Apart from the role of hæmolysis in the causation of the acute renal failure, it is not clear to what extent the ingestion of a large amount of analgesic may have directly contributed to the kidney damage, as proteinuria, hæmaturia, oliguria, anuria, azotæmia and acute tubular necrosis have been described in man following the administration of salicylates (Prescott, 1966). Chronic analgesic abuse may have played some part in the genesis of the renal failure by impairing the blood supply to the renal papillæ (Kincaid-Smith *et al.*, 1968). However, the patient repeatedly denied regular analgesic ingestion.

The excretion urograms taken 5 months after the acute illness showed the characteristic appearances of papillary necrosis. Although the radiographs taken at the time of the renal failure showed insufficient detail to decide whether or not there were papillary lesions at that time, the renal biopsy showed no microscopic evidence of chronic interstitial nephritis. These findings in conjunction with the absence of clinical evidence of chronic analgesic abuse, suggest that the massive papillary necrosis may have occurred at the time of the acute renal failure as the result of the combined effects of ischæmia leading to acute tubular necrosis and the large amount of analgesics ingested.

The diagnosis of G6PD deficiency is difficult in the presence of hæmolysis. During hæmolysis the older cells are destroyed first and as the red cell content of G6PD falls with cell age, all tests for G6PD deficiency will give normal results in the presence of a largely young red cell population. This difficulty in diagnosis was increased in the present case by the blood transfusion and by the persistent reticulocytosis during the recovery phase. Recently Herz *et al.* have shown that this problem of establishing the diagnosis during a hæmolytic episode may be overcome by separating old from young cells by density gradient centrifugation (Herz *et al.*, 1967).

The reversible sideroblastic anæmia observed was associated with a defect in hæm synthesis as evidenced by the finding of siderocytes, Pappenheimer bodies and " ring " sideroblasts. A few cases of sideroblastic anæmia associated with chronic phenacetin abuse have been documented (Dacie and Mollin, 1966; McMillan *et al.*, 1968) but this has not been described as a complication of acute analgesic overdosage. The rarity of these cases suggests an individual idiosyncrasy. We suggest that a genetic defect in hæm synthesis is responsible. Evidence of such a genetic susceptibility has recently been found in a case of sireroblastic anæmia associated with antituberculous therapy (Bateman, in preparation).

The slow hæmatological recovery of this patient was probably mainly due to the sideroblastic anæmia and to a lesser extent to the gastro-intestinal blood loss.

Pharmacogenetics is rapidly becoming an important aspect of clinical medicine. In this case G6PD deficiency, sideroblastic anæmia and possible renal tubular susceptibility (Prescott, 1965) were revealed as a consequence of the ingestion of a large dose of an analgesic preparation.

SUMMARY

A case is described of a West-Indian Negro male with glucose-6-phosphate dehydrogenase deficiency who developed acute intravascular hæmolysis, renal failure and reversible sideroblastic anæmia, following an overdose of Codeine Compound tablets. The renal failure was successfully managed by peritoneal dialysis. Generalised renal papillary necrosis was found on pyelography 6 months later and it is suggested that this may have been conditioned by and occurred at the time of the acute renal failure. Problems regarding the diagnosis of G6PD deficiency following acute hæmolysis are discussed and the possible pathogenesis of the transient sideroblastic anæmia observed in the patient is considered.

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EARLY ARABIAN UROLOGISTS

A Historical Review

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Anyone fortunate enough to visit modern Egypt and the teaching hospitals of Alexandria and Cairo, cannot but become aware of the abundance of urological pathology which is apparently endemic in the Arab countries. It is, therefore, not surprising that much of our earlier knowledge of urology stems from the accurate observations of early Arab physicians. At Sakkara, near Cairo, archæologists are now hoping to uncover the tomb of Imhotep (*c.* 2800 B.C.), the world's first recorded physician: buried with him may lie instruments and medical treatises originating some 4,700 years ago.

The Arabs inherited a form of medicine from the Persians, Indians and Greeks and were greatly affected by the spirit of Hippocrates and the teachings of Galen. In Egypt, during the Arab period, the Abbassin Khalifs encouraged translators of the quality of men such as Honein Ibn Issac al-Abaddy (A.D. 810-877), who studied Latin in Alexandria and subsequently practised medicine in Baghdad. Soon, Arab medicine reached its peak of fame, and students from the East and West flocked to Cairo, Baghdad and Damascus to study in this so-called medical Renaissance, which lasted from the eighth to the eleventh centuries, A.D.

Much that might be known about these early Arab physicians remains, untranslated, in manuscripts in the Egyptian Museums. This paper sets out to give a brief insight into the historical background of some of them, together with references to some of their observations as applied to Urology. The original manuscripts, most of which lie in the Cairo Library, have each been carefully studied by the principal author (M. A. R) and subsequently translated into Engish.

Aly ibn Rabun al-Tabary (*c.* A.D. 850)

Al-Tabary, a physician who combined his early Greek training with later Indian studies before settling to practise medicine in Baghdad, wrote the first real Arab textbook of Medicine, *Ferdos al Hekma* (" The Paradise of Wisdom "), in A.D. 850. This book is divided into four parts, each of which is subdivided into essays: one of these deals specifically with urological problems.

In it, he attributes urinary incontinence to " either weakness of the bladder wall or to inflammation producing such severe tenesmus that the patient cannot hold on to his urine ". Retention of urine he considered to be due to " various causes such as inflammation of the penis, thickening of the muscles at the bladder outlet, local disease in the nearby gut, inability of the bladder wall to contract, or, sometimes, merely to direct obstruction of the urinary channel by stone or pus ". He also recognised that some retentions were due to " diseases affecting the nerves in the vertebræ ". In differentiating bladder atony from obstructive retention, he recommended that " if there is a rounded swelling in the suprapubic region, the bladder is full of water, and if you press on the bladder by hand and no urine escapes, the swelling is due to obstruction and not to weakness of the bladder wall ". His descriptions of the clinical picture of bladder stone are quite masterly, and he found that the condition was commoner in children than in adults. His treatment of stone obstructing the bladder outlet consisted of " laying the child on its back, raising both legs and shaking them vigorously to disimpact the stone ". Also, although unable to appreciate the reasons for his observations, he was apparently the first man to describe accurately abnormalities in the naked-eye appearance of human semen.

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Thabet ibn Kurrah (A.D. 836-901)

Ferdos al Hekma was subsequently replaced, in the Arabian medical schools, by *Al Zakhira Fe Elm el Teb* ("The Treasure in Medical Science") which was written by Ibn Kurrah, another Baghdad physician, with 31 chapters, one of which deals specifically with urology.

Ibn Kurrah attributed stone formation in the kidneys and bladder to " narrowing of the outlet and acute inflammation ", and was the first to point out that excessive urination had other causes besides diabetes.

Abou Bakr Mohammed ibn Zakareya al-Razy (A.D. 850-924)

This man, known to Europeans as Raziz, was the father of clinical medicine in the Middle East. Born in the city of Rai, in Iran, he studied under al-Tabary, became director of the Rai hospital and was finally appointed head of the Baghdad hospital.

He was the first to record the use of silk thread for suturing wounds, and recommended that " every physician should reassure his patients of good health and of further improvement, even when he himself is not sure of it ". He firmly believed in personal clinical tuition, and taught that " the art of medicine, as presented in books, is much inferior to the practical experience of a skilful physician ", whilst, at the same time, showing himself to be a far-sighted philosopher when he advised that " patients should depend on one reliable physician, for those who visit many physicians are liable to become victims of the faults of each of them! "

Raziz was a prolific author on scientific subjects, and wrote no less than 56 texts on Medicine alone. For centuries, his classical textbook *The Continent* was considered the standard work on Medicine, and both the 7th and 8th volumes are devoted entirely to Urology. He accurately described acute pyelonephritis, and advised that " all men with blood and pus in their urine should be asked about loin pains, rigors and irregular fever". He was also among the first to differentiate renal pain from bowel colic, and gave a detailed description of the operation of perineal lithotomy. He also advised that " if the stone is bigger than the incision, it should be crushed with a lithotrite ", thereby showing that stone-crushing was carried out some 1900 years before the usually accepted origin in the eighteenth century. At that period of time, however, the lithotrite was passed through a perineal incision; in the eighteenth century it was first introduced via the urethra. He treated impacted urethral calculi by " direct incision over the stone, having first tied the penis proximally and distally to the stone; the former to prevent the stone slipping back into the bladder, the latter being applied after first pulling downwards on the penile skin so that later retraction of the intact skin would cover the urethral incision ". He described, in considerable detail, the complications of cystostomy; for wound bleeding he recommended " packing it with incense, crushed vitriol and a fluff of cotton dipped in vinegar and water ". Like al-Tabary, he clearly distinguished between the clinical signs of urinary retention and anuria, and he gave a particularly vivid account of the features of scrotal gangrene. Although unaware of the condition of hæmoglobinuria, he described a typical case " with urine the colour of the water in which meat is washed but in which there was no possible cause such as bladder ulcer, stone or bleeding vessel ", the change in urine colour being attributed to " destruction and dissolution of the body ". In yet another of his books, entitled *The Booklet of Mansoury*, he detailed the physical characteristics of urine, and correlated these changes with different diseases.

Abu al-Kasem Khalaf al-ZahraWy (A.D. 936-1013)

Born in Spain, al-Zahrawy, known to Europeans as Abulkasis, was probably the most famous Arab writer on purely surgical topics, and his book *Al Tasreef*, comprising 30 volumes, dealt in detail with the, then, new science of surgical anatomy. Chapter II contains no less than 14 articles on urological topics incuding congenital meatal stenosis which he treated by " incision followed by the insertion of a fine nail, made of lead, for three or four days in order to maintain the new width ". He recommended that the nail be removed during micturition and immediately replaced. Circumcision is also dealt with in some detail, and he devised a special syringe for washing out the bladder (Rifaie, 1968). He also devised special instruments for the operation of perineal lithotomy, and described, in considerable detail, the technique and complications of this procedure. For stones impacted in the penile urethra he devised a sharp-pointed instrument which, by using a rotary movement like a corkscrew, pierces the stone which, in turn, is prevented from slipping back into the bladder by a " ligature tied round the penis proximal to the stone " (Rifaie, 1968).

Al-Zahrawy appears to have been the first man to recommend cutting for stone in women, removing it through an inguinal incision. In dealing with the, then, reticence to any examination of a woman by a male physician, he recommended that " you bring a mid-wife and order her to obey all your orders. If the patient is a virgin, the mid-wife should introduce her finger into the rectum to search for the stone; when she has found and immobilised it under your finger, you will then order her to incise over it. If the patient is not a virgin, order the mid-wife to introduce her finger into the vagina and to search for the stone after placing her left hand over the bladder and compressing it strongly. When she has found it, she should push it away from the bladder neck downwards as far as it will go until it reaches above the upper part of the thigh. She will then incise over it, but her finger will not leave the stone and will compress it. The incision should be a small one at first, then she will introduce a sound through the small incision, and if she feels the stones she should enlarge the incision as much as she would judge it necessary for the stone to come out."

Aly ibn al Abbas al-Magousy (*c.* A.D. 944)

Al-Magousy, a Persian physician of considerable renown, wrote *Kamel al Sennaha al Tabbeia* (" The Royal Book "), consisting of two large volumes covering, between them, the entire scope of Medicine in that era. He was the first man to describe capillary networks, and wrote freely on pulmonary tuberculosis and laryngology. The third essay of Volume I is devoted to the anatomy and physiology of the urogenital tract, and includes far-sighted views on the valvular action of the ureteric orifices. He believed that " the penis, during coitus, functioned through the action of two opposing muscles pulling in opposite directions so that the urethra became straightened-out. At the same time, the spermatic channels were similarly straightened out and, by becoming wider, allowed spermatic fluid to pass rapidly and easily." He describes the function of the prepuce in men as being the same as the clitoris in women, and noted that " in women, the testicles are rounded and hard, while in men they are elongated and soft ". Such descriptions could apparently only have come from observations of autopsy dissection, but Brown (1964) states that, at that time, the autopsies were only carried out in monkeys, because Yohanna Ibn Maswey could not obtain human bodies. Brown suggests that Yohanna and others based all their views on human functions by interpolating their findings in animals. One long essay in the second volume is devoted entirely to the treatment of urological conditions. In it, he advises the need to have different sizes of catheter available in the treatment of urinary retention, and he also gives a description of the technique to be used in passing silver catheters through the curved urethra which would merit inclusion in any modern textbook. Perineal cystotomy, external urethrotomy and orchidectomy are all described in detail, as are the operations for hydrocele and excision of varicocele. Perhaps most surprising of all, he discusses the management of hermaphroditism and hypospadias.

Abu Ali el Hussein ibn Abdallah ibn Sina (*c.* A.D. 1037)

This man, best known to most Europeans as Avicenna, was undoubtedly one of the greatest philosophers and physicians in the early part of the eleventh century. Born in Iran, he wrote his *Cannon Medicine*, a textbook that was to become the principal work of reference throughout the universities of France and Italy. Such was his undying fame that his portrait still hangs in the Great Hall of the Paris Medical Faculty.

Although his greatest scientific observations were focused on jaundice, meningitis, facial palsy and concussion, Volume I contains some far-sighted views on urinalysis. In it, he stresses that " one should not trust the findings of an examined sample of urine unless it should be fresh, and preferably taken from the first urine voided in the morning ", and he advised against sexual intercourse and the eating of pomegranates before submitting urine for testing, because both changed its colour. He believed that " urine should be placed in a transparent glass or crystal pot, and should be kept away from excess heat and cold ". It should also not be left for a long time before examination, otherwise " its characteristics may change ".

In Volume II he gives beautiful descriptions of renal and ureter colic. He then goes on to compare the pain of upper-tract stone with that of bladder stone, and, in detailing an account of the operation for bladder stone, he advises " considerable acquaintance with bladder anatomy, particularly the site of junction of the spermatic channels and the blood supply of the area, in order to prevent subsequent fistulæ, sterility or excessive bleeding ".

Avicenna was also the first man to recommend the use of soft malleable catheters made of leather.

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POST-PROSTATECTOMY MANAGEMENT—A NEW CATHETER SYSTEM

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APART from general management, care of a patient following prostatectomy is mainly concerned with ensuring uninterrupted drainage of urine and blood from the lower urinary tract until natural hæmostasis is attained, avoiding accumulation of blood and the risk of consequent clot retention. This complication, if it occurs, involves the patient and staff in tedious and, for the patient, often exhausting attempts to re-establish drainage by bladder washouts, or even, necessitate returning the patient to the operating theatre for Bigelow evacuation of clots or cystotomy under anæsthesia.

Whatever method of prostatectomy is used the immediate operative end result to be dealt with is the same, *viz*. a bleeding prostatic cavity bounded by a so-called false prostatic capsule communicating with a bladder cavity—2 cavities, one shedding blood and the other draining urine.

For this purpose a catheter is commonly used for drainage of urine and blood, the aim being to avoid giving blood shed in the prostatic cavity the opportunity to clot and obstruct the catheter lumen; to the same end irrigation is often resorted to.

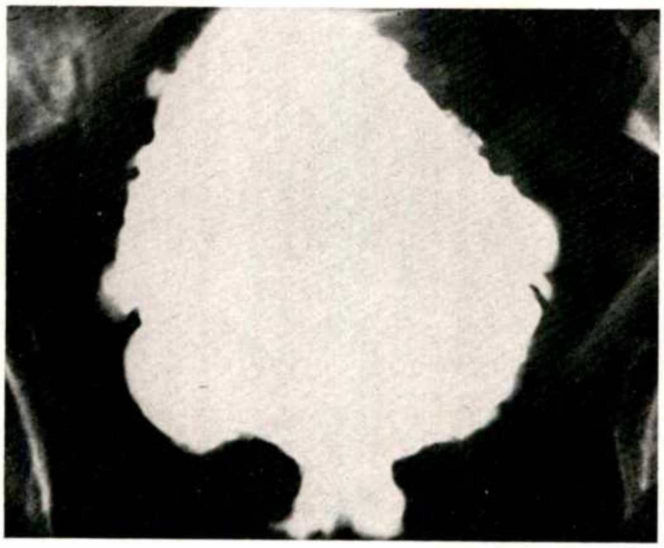

FIG. 1
After prostatectomy the prostatic cavity acts as a sump for which direct dependant drainage would appear to be indicated.

Conventional catheter management makes no special provision for the prostatic cavity as irrigation and drainage takes place at the level of the bladder and when a self-retaining catheter is used owing to the disposition of the ports above the inflatable ballon at a relatively high level in the bladder; accordingly the prostatic cavity must act as a sump (Fig. 1) in which blood, blood clot and urine accumulates overflowing up into and then draining from the bladder secondarily after passing around the retaining ballon; because of the time lapse between shedding and run-off there is increased opportunity for blood clotting to occur with the risk of obstructing drainage.

Again it is suspected that this sump effect of the prostatic cavity contributes to establishment of infection in the lower urinary tract following prostatectomy delaying healing and retarding hæmostasis; all in all a state of affairs best avoided.

With the relative shortage of nursing staff in hospitals there is much to be said for a system of post-prostatectomy management which is safe and simple and which combines the minimum need for attention with maximum avoidance of complications.

A catheter system has been designed to meet these requirements and overcome the objections to conventional catheter management that have been indicated; it introduces a principle that treats the operation area as 2 distinct cavities, the bladder draining urine and the prostatic cavity shedding blood, provision being made for each in the catheter construction in that there is special provision for the prostatic cavity to be irrigated and or drained directly.

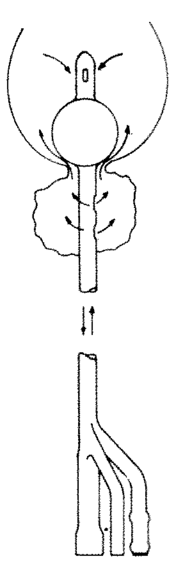

Fig. 2
Catheter version A.

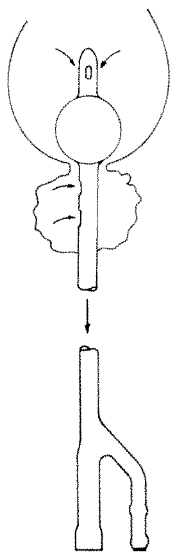

Fig. 3
Catheter version B.

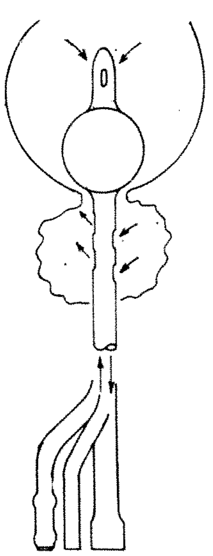

Fig. 4
Catheter version C.

There are 3 versions of this catheter which is an inflatable balloon self-retaining type.

A. A 3-way version with the irrigating channel bearing 2 lateral ports below the balloon so that when the inflated balloon is in the bladder the irrigating ports open into the prostatic cavity.

Irrigation fluid (sterile normal saline) introduced at a continuous drip rate into the irrigating channel from a gravity container passes directly into the prostatic cavity where it meets blood freshly shed dilutes it and carries it with a flush action into the bladder from whence it drains to the exterior (Fig. 2).

B. A 2-way version with a drainage channel only bearing 2 lateral drainage ports below the balloon acting at the level of the prostatic cavity as well as drainage ports at the tip via which the bladder drains. This catheter can be intermittently irrigated via a Y-shaped connection if desired (Fig. 3).

C. A 3-way version which combines the features of A and B; both the irrigation and drainage channels bear 2 side ports below the balloon acting at the level of the prostatic cavity which is therefore irrigated and drained directly (Fig. 4).

D. These 3 versions A, B and C are made with either a 30 ml. capacity inflatable balloon for use when the bladder neck is sutured in the Harris or Hrynschak manner. (Tinckler, in press), or a 75 ml capacity balloon for use when the bladder neck is left open after enucleating the prostate; the large balloon version ensures that the balloon remains in the bladder and is kept out of the prostatic cavity permitting the application of this catheter irrigation drainage system to all types of prostatectomy.

The retaining balloon is electively positioned in the bladder as opposed to the prostatic cavity in the belief that contraction of the prostatic capsule and collapse of the cavity are significant factors contributing to spontaneous arrest of bleeding and therefore should not be prevented or interfered with by the presence of an inflated balloon.

TABLE

Urine Culture in Consecutive Cases using the Prostatic Cavity Irrigating/Drainage Catheter

Case	Pre-operative Urine Culture	Operation	Post-operative Urine Culture				
1 J. R.	*E. coli*	Prostectomy*	*E. coli*	No growth	*E. coli*		
2 T. M.		Prostectomy	No growth	No growth	No growth		
3 R. M.		Prostectomy	No growth	No growth	No growth		
4 F. M.	No growth	Prostectomy	*E. coli*	No growth	No growth		
5 W. T.		Prostectomy	No growth				
6 W. S.		Prostectomy	No growth	No growth			
7 G. B.		Prostectomy	No growth	No growth	No growth		
8 W. Y.		Prostectomy	No growth	*E. coli*	*E. coli*	No growth	
9 E. H.		Prostectomy	No growth	No growth	*E. coli*		
10 C. B.		Prostectomy	No growth	No growth			
11 L. M.		Prostectomy	*E. coli*	No growth			
12 G. R.		Prostectomy	No growth	Citrobacter			
13 J. C.		Prostectomy	No growth	Staphylococcus			
14 H. P.		Prostectomy	No growth	No growth	No growth	Micrococci	No growth
15 C. A.		Prostectomy	*E. coli*	No growth	No growth	No growth	
16 A. A.		Prostectomy	No growth	Micrococcus	No growth	No growth	

* Followed by nephrectomy for long standing pyonephrosis.

An impression gained from the use of this catheter is that with provision being made for direct prostatic cavity drainage which prevents pooling of blood and debris, a cleaner urinary tract is maintained after prostatectomy with consequent benefit to post-operative recovery; the rôle that this new catheter system may play in the avoidance of post-operative infection is presently under investigation (see Table).

The gravity container, connecting tubing, prostatic cavity irrigating drainage catheter and disposable plastic drainage bag constitute a closed system which mitigates the risk of infection being introduced.

The behaviour of these catheters *in situ* has been studied radiologically with an image intensifier using radio-opaque irrigating fluid and their action in respect of the prostatic cavity confirmed.

Radiological Study.—The circulation of irrigating fluid and the drainage characteristics of each version of this catheter system were investigated radiologically in a number of patients variously on the 3rd to the 5th post-prostatectomy day. Radio-opaque fluid (25 per cent Hypaque) was substituted for the saline irrigation fluid; its progress was observed by means of an image intensifier and the observations recorded on 16 mm. ciné film.

The observations are summarised as follows:

> *Version A.*—The fluid was seen to travel up the irrigation channel, emerge into the prostatic cavity then enter the bladder via the bladder neck alongside the catheter, outline the retaining balloon and run out down the drainage channel (Fig. 5).

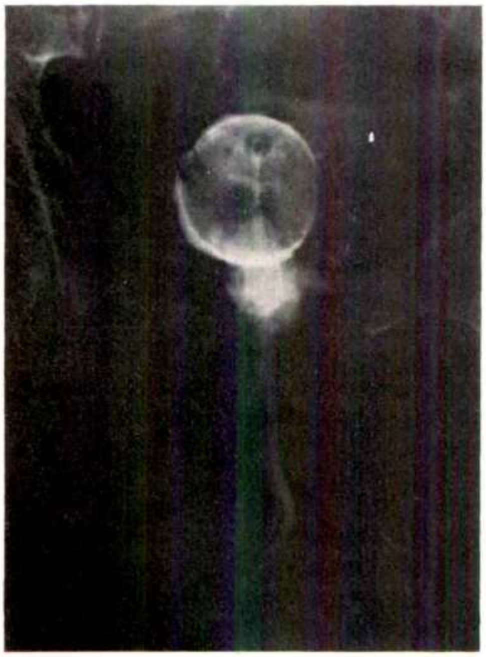

FIG. 5
Radiological study of catheter version A.

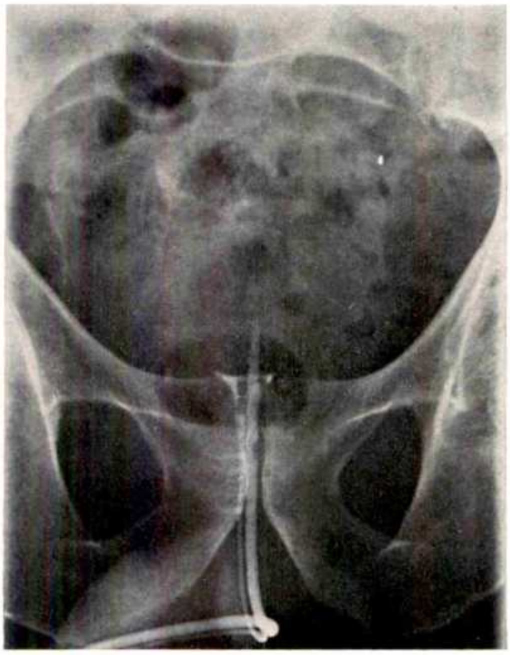

FIG. 6
Radiological study of catheter version C.

> *Version C.*—The fluid passing up the irrigation channel emerged into the prostatic cavity, did not enter the bladder, but passed into the drainage channel, draining to the exterior and refluxing a little up the drainage channel in the direction of the bladder (Fig. 6).

Made in latex rubber these catheters can be obtained in a range of sizes from William Warne & Co. Ltd., Barking, Essex, and in Simplastic from J. G. Franklin & Sons Ltd., Lane End Road, High Wycombe, Bucks.

A 16 mm. film in colour and with an optical sound track commentary demonstrating the use of this catheter system has been prepared; and is available in the B.M.A film library.

A patent application has been filed.

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GENITAL FUNCTION IN MALES WITH VESICAL EXSTROPHY AND EPISPADIAS

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The importance of achieving continence in bladder exstrophy and epispadias patients resulted in a concentration of attention on the urinary tract: the genital tract usually receives second consideration. In this paper we are reporting on the sexual abilities and the potential fertility of these patients in order to plan operative repair with the object of attaining satisfactory genital function as well as control of urinary incontinence, whether the latter is to be achieved by functional reconstruction or by diversion.

The apparent normality of the testicles, and the integrity of the genital tract up to the verumontanum, makes it unlikely that many of these cases will have a congenital failure of spermatogenesis. They might clearly suffer from inflammatory changes at the exposed verumontanum, but more probably attempts to reconstruct the urethra might obstruct, or even sever, the genital passages. Biochemical changes consequent upon renal damage due to ascending infection might also interfere with testicular development. This review has been made with all these factors in mind. The number of cases available was small and no statistical conclusions are possible, but there was sufficient information to indicate the likely trend of events.

Materials and Methods.—The material studied comprised 16 male patients who had suffered from ectopia vesicæ and 15 males with complete epispadias. All except one were operated upon at The Hospital For Sick Children, Great Ormond Street, between 1945 and 1953. Various surgeons had been concerned and various methods employed in their initial treatment, but the senior author had been involved at some stage. The patients were asked to come into the Shaftesbury Hospital for the day for clinical assessment. This entailed the following: Clinical examination with particular attention to the genital tract. Semen analysis, repeated when indicated. Blood count and chemistry. Intravenous pyelogram. Urethral exploration with probe and urethrogram in patients who had difficulty in ejaculation or complained of urethral discharge.

Testicular biopsy was not performed even when the seminal fluid showed absent sperms, although it would have been helpful in differentiating between obstructive azospermia and defective spermatogenesis, as we felt it would be of academic interest only.

The seminal fluid was examined according to the standard method. (Hotchkiss, 1970). The necessary precautions were taken as regards previous ejaculation and collection. The test was not repeated on patients who produced normal specimens. On those patients with oligospermia or aspermia, the test was repeated 3 or 4 times.

We ensured that the patients did not receive any drug which might have inhibited spermatogenesis, such as Nitrofurantoin, antidepressants or hormones (Amelar, 1966), and there was no history of mumps, recent illness, operation or prolonged fever, factors which can depress testicular function, in any of our patients. Also, none was subjected to irradiation other than routine intravenous pyelogram examination every 3 or 4 years.

Assessment of chordee was based on:

1. Patient's statement with regard to state of erection and success or otherwise of attempted intercourse.
2. Clinical examination.

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Particular attention was made to the site and size of the external meatus, the testicles and the prostate.

Results: Exstrophy Cases

1. *Erection.*—All patients achieved good erection. Ten patients experienced satisfactory intercourse, 3 of whom are recently married. The relatively short, broad phallus was not a handicap in spite of a minor degree of chordee in 2 patients.

The penile deformity in bladder exstrophy is (*a*) retraction of the penis, partly due to the short urethral strip and partly due to the tethering of the corpora to the pubic bones, which are widely separated, and (*b*) the lack of urethral tube. Surgery aims at correction of chordee and formation of a seminal conduit. All our patients had reparative surgery during infancy or childhood. However, on examination as adults:

Five patients had no chordee.
Two patients had minor chordee.
Two patients had moderate chordee but were not unduly concerned about it.

Seven patients had chordee requiring surgery. These patients were operated upon either as adolescents or as adults and it was noted that abdominal wall scarring, especially at the root of the penis, was partly, and in 3 patients totally, responsible for chordee. The symphyseal gap remained as wide as ever. Incidentally, none of the patients in this series had any orthopædic disability.

We found that chordee repair in these adult patients required 2 basic steps—excision of scar tissue holding the penis upwards, followed by filling of the skin gap, which could be achieved by using a flap of scrotal skin.

Over the last 10 years, the senior author's policy has been to perform a penile lengthening procedure during the first year or 2 of life before proceeding to either functional reconstruction or urinary diversion. Penile lengthening was achieved by V-Y plasty (Fig. 1,A). Recently we have tried inverted V-Y plasty instead (Fig. 1, B) on several occasions. It is felt that the second procedure may be better because it is less likely to injure the verumontanum and ejaculatory ducts.

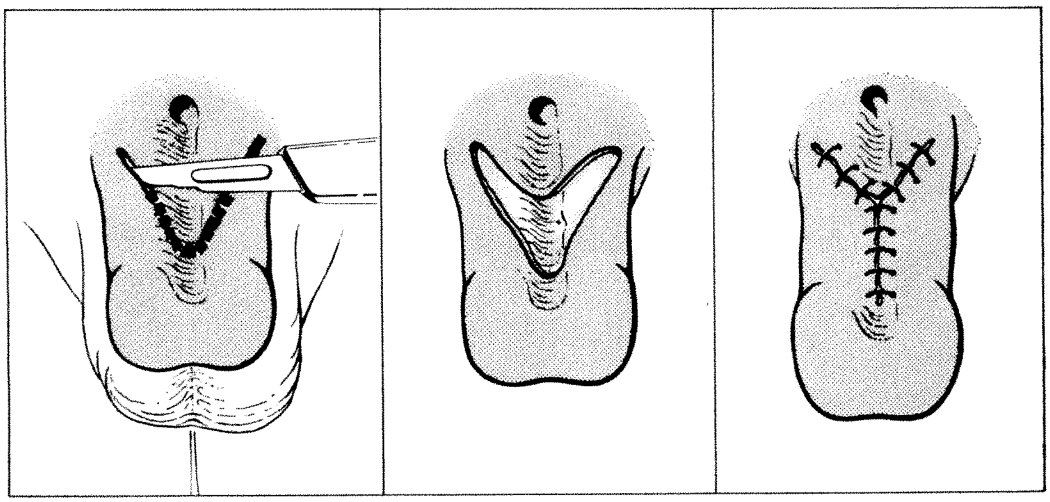
2. *Ejaculation.*—Twelve patients ejaculate normally. One patient does not ejaculate (Case 4). Patient 14, who had previous bladder closure attempted during infancy with transposition of the urethra so that the external meatus was in the perineum, did not achieve continence and the ureters were transplanted into the colon resulting in incontinence of both fæces and urine. This did not improve over the following year and he developed prolapse of the rectum so that an ileal loop diversion was undertaken. As an adult he is married, experiences satisfactory orgasm, but there is no ejaculation; instead the semen oozes out slowly from the perineal meatus on straining or sneezing some 15 to 20 minutes after intercourse. A probe could not be passed into the hypospadiac meatus for more than a few millimetres. Attempts at urethrography failed as the medium could not be injected. At operation the urethral strip was dissected out and found to be severely kinked 1 cm. proximal to the meatus with a stricture at this point. The bladder was opened and was found to be of small capacity but there was adequate development of the prostate: the urethra was laid open in the perineum. Six months later he stated that there was no improvement in ejaculation. As his seminal fluid volume was 1·5 ml. and there were only 3 million sperms/ml. showing 71 per cent abnormal forms and low motility, as well as excess pus cells, it was felt that not much was to be gained by reconstruction of the urethra.

Patient 15 had had excision of the bladder mucosa, transplantation of the ureters into the colon and the urethra had been tubed. However, infection of the suture line left him with an external meatus on the dorsal aspect of the penis, almost at the root of the penis. As an adult he complained of blockage of the seminal fluid after ejaculation, and he had to massage the semen out. On examination the external meatus was stenosed. Semen analysis was subnormal.

Meatoplasty was performed. Six months later the urethra was tubed. The seminal fluid improved in quality and the seminal flow improved as well. The count and volume were raised to normal standards, possibly because of better collection.

The last patient in this series is similar to patient 14. He complained of ejaculation a few minutes after orgasm. His external meatus was in the perineum. He was not investigated any further.

1a. Penile lengthening – V-Y plasty



1b. Penile lengthening – inverted V-Y plasty

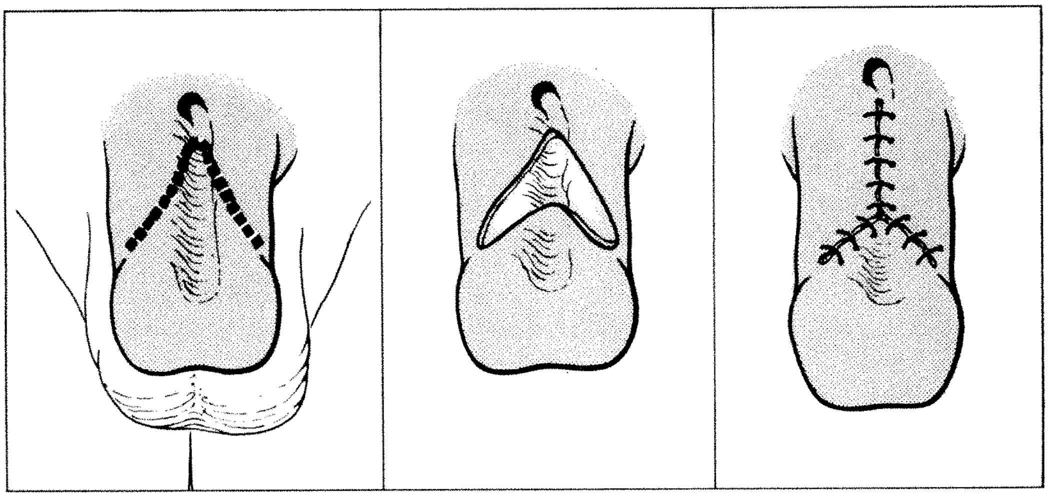


FIG. 1

A, Penile lengthening, V-Y plasty. B, Penile lengthening, inverted V-Y plasty.

In the 4 patients where the external meatus was in the perineum, 3 had difficulty with ejaculation and 1 did not ejaculate. It was clear that transposition of the urethra to the perineum to correct chordee was an unsatisfactory procedure which could result in obstruction due to stenosis or kinking of the tube.

Ejaculation is a reflex stimulated by pressure of semen in the urethra. It requires intact pudendal nerves and contraction of the perineal muscles as well as contraction of the internal urethral sphincter and relaxation of the external sphincter (Hotchkiss and Fernandez-Leal, 1957). In bladder exstrophy and epispadias the bladder neck is scarcely formed at all, retrograde ejaculation is therefore likely should bladder neck repair fail, and may contribute to sterility or defective ejaculation in these patients, particularly when the distal urethra is obstructed.

3. *Semen Analysis.*—Investigation was undertaken in 8 cases who had undergone attempts at functional reconstruction of the bladder. One patient only produced a normal seminal specimen, but with excess pus cells. Three patients had severe oligospermia (the count being between 1 and 6 million sperm/ml.). The sperms were of poor motility and viability, as well as showing a large number of abnormal forms, mainly abnormal heads rather than tails. Three patients failed to show sperms in their ejaculate on repeated tests. The 8th patient experienced orgasm but did not ejaculate.

TABLE I

Semen Analysis in 16 Bladder Exstrophy Patients

Functional Closure in 8 Patients	Urinary Diversion and Excision of Mucosa in 8 Patients
One patient produced normal specimen except for excess pus cells.	Four patients produced normal specimens.
Three patients have severe oligospermia. The sperms are poorly motile and excessive abnormal forms. One patient has excess pus cells. Sterile on culture.	Four patients have a variable degree of oligospermia, poor motility and excess abnormal forms. Two showed excess pus cells.
Three patients have absent sperms in their ejaculate.	
One patient experiences orgasm, but does not ejaculate.	

TABLE II

Fertility in Bladder Exstrophy Patients

Normal fluid	5 patients
Absent sperms in the fluid	3 patients
Absent ejaculation	1 patient
Low count (less than 20 million/ml.). Sluggish motility and excess abnormal forms. (Abnormal heads and tails more than 40% McLeod 1953)	7 patients

Semen analysis was also performed on 8 cases in whom no closure had been attempted. They had been considered suitable only for urinary diversion and excision of exposed bladder mucosa. Four produced normal semen specimens and four produced subfertile specimens (Table I).

The final score was:

Out of 16 patients only 5 produced normal seminal specimens and 11 produced specimens incompatible with the probability of conception (Table II).

In 3 patients there was azoospermia and 1 patient does not ejaculate. These 4 patients form an interesting group.

Case 1.—The bladder was closed, the patient remained incontinent and a uretero-colic transplant was undertaken. Ten years later he complained of a persistent greenish urethral discharge. Urethrograms outlined a seminal collection in the defunctioned bladder (Fig. 2). Cystectomy was performed, resulting in cessation of the discharge but his seminal fluid now contains no sperms.

Case 2.—Functional closure was attempted. There was a breakdown of the suture line with gradual re-establishment of exstrophy. Reclosure was undertaken. However, he remained incontinent and a uretero-colic transplant was performed, but because of continuous acidosis the colonic loop draining the ureters was excluded to form a conduit towards the abdominal wall. This procedure was performed at the age of 15 years so that he was chronically acidotic during puberty. His seminal fluid contains no sperms, instead there were cells which resembled sperm precursors. His testicles are clinically normal. His defunctioned bladder is still *in situ*.

Case 3.—Bladder closure at 3 years, still incontinent. One year later the urethra was transposed to a hypospadiac position in the perineum in an attempt to allow good chordee correction. Two years later a fascial sling operation was performed to tighten the bladder neck. He remained incontinent. The bladder remains *in situ*. Semen analysis showed absent sperms.

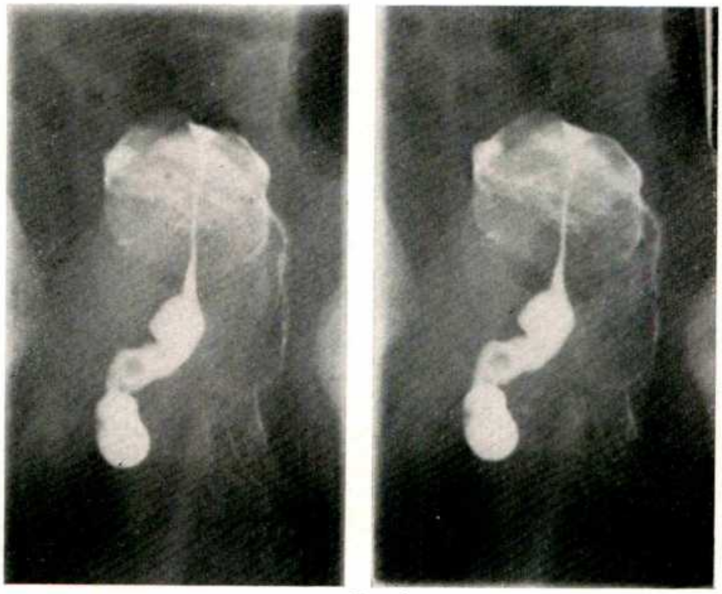


FIG. 2

Urethrogram, the dye outlined a seminal collection in the defunctioned reconstructed bladder.

Case 4.—Closure of ectopia vesicae was attempted twice. The urethra was transposed to the perineum with satisfactory continence. However, he continued to form stones in the closed bladder. The stones were removed twice. Finally the bladder was incompletely excised and he had a uretero-colic transplant at the age of 4 years. Five years later he complained of a persistent foul white discharge per urethram. X-rays showed more stones. At operation these were found to be in the bladder remnant. Excision was difficult but complete. The discharge ceased, but he does not ejaculate. The external meatus looked patent but the patient refused to have urethrograms or any further examination.

4. *Herniæ and Undescended Testicles in Bladder Exstrophy*:—Four patients have unilateral inguinal herniæ, which were repaired during the first year of life. Two patients subsequently produced normal seminal specimens and 2 were abnormal.

Two patients had bilateral undescended testicles which were brought down to the scrotum at the ages of 5 and 6 years. Both produced subnormal seminal fluid. One patient had testicles of soft consistency and smallish size.

5. *The prostate in Bladder Exstrophy*.—The prostate was of normal consistency in all patients. It was rather small in size in 4 patients. Two produced normal seminal fluid.

Results: Epispadias Cases

All 15 patients were born with complete epispadias. Bladder neck repair was performed by Young's procedure (Young, 1937) or by fascial sling. The urethra was tubed after release of chordee by some form of plastic procedure.

1. *Erection.*—All 15 patients get good erections. Eleven copulate satisfactorily. On examination the 11 patients had no chordee. The repair was satisfactory, the external meatus was on top of the glans. Two patients required further chordee correction and advancement of the external meatus distally. The suture line broke down due to sepsis in the first procedure. One patient first presented when 21 years old (see later).

2. *Ejaculation.*—All patients except 1 ejaculate normally. One patient with an ileal bladder ejaculated through a suprapubic sinus. He failed to attend for further investigations.

3. *Semen Analysis.*—Nine patients produced normal specimens. Three of these patients had successful bladder neck repair. The other 6 patients had ureters transplanted into the colon and in 3 patients this was later converted into a colonic loop. Four patients produced subnormal specimens, low counts, sluggish motility and excessive abnormal forms.

The patient who tolerated the deformity for 21 years had a two-stage procedure. The first stage was chordee correction by V-Y plasty. Six months later Young's bladder neck repair and rolling of the urethra were performed. This resulted in reasonable urinary continence. However, semen analysis before and after surgery showed few non-motile sperms. It is conceivable that his verumontanum being exposed for such a long time had been subjected to repeated minor trauma, low grade infection, or both.

4. *Testicles and Prostate.*—Testicles and prostate were clinically normal in all patients.

DISCUSSION

This review has made it clear that in order to achieve a satisfactory erection without chordee, surgical correction is necessary both in exstrophy and in epispadias, and that full correction may not be easy to obtain at one stage in early childhood. As far as the semen is concerned, however, the chief danger to fertility appears to lie in attempts at reconstructive surgery which may damage the verumontanum or obstruct the urethra. There is particular danger in cases of exstrophy of the bladder where reconstruction has been attempted and then a diversion performed. In the absence of urine descending through the urethra a severe stricture can form without causing symptoms. It is only after puberty that the presence of the stricture is recognised and by the time it is treated there may have been irreversible damage to the genital system.

We intend in future to continue some attempts at functional reconstruction of the urinary tract, but with greater emphasis on the need to preserve the male genital tract. If, however, a primary diversion is performed for exstrophy it seems wise to leave the urethral reconstruction until after puberty. In epispadias chordee correction is necessary but there is very much less danger of damage to the verumontanum or of obstruction to the newly formed urethra.

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THE DIAGNOSIS AND MANAGEMENT OF BACTERIAL PROSTATITIS

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The diagnosis of " prostatitis " is often made by the physician, but rarely is substantiated in the laboratory. Unfortunately, most clinicians base their diagnosis upon the medical history, physical examination, urinalysis, and microscopic appearance of the expressed prostatic secretion. These indirect diagnostic parameters have led to considerable confusion regarding the nature and clinical significance of prostatitis. Indeed, previous data have been so poor that O'Shaughnessy *et al.* (1956) and Gonder (1965) have questioned the existence of bacterial prostatitis.

A few years ago we designed quantitative bacteriologic culture techniques to confirm the diagnosis of bacterial prostatitis in the laboratory (Meares and Stamey, 1968). Our experience with these techniques suggests that chronic bacterial prostatitis is a major source of relapsing urinary tract infection in men.

In our experience bacterial prostatitis is an infection of the prostate gland caused primarily by gram-negative organisms. Approximately 80 per cent of our cases have been due to various strains of *escherichia coli*; The remaining 20 per cent include cases due to *klebsiella-aerobacter*, Proteus (primary *P. mirabilis*), and *Pseudomonas* species. Mixed infections (two or more pathogens) have been found in only 15 per cent of our cases. Although other investigators implicate gram-positive organisms in bacterial prostatitis, our data suggest that only gram-positive infections due to *streptococcus fecalis* produce significant morbidity. Tuberculous prostatitis is still found in patients who have renal tuberculosis. Since the advent of antibiotics, however, gonorrheal prostatitis is apparently less prevalent. The rôle of obligatory anaerobes in prostatitis has not been defined.

Pathology.—Acute bacterial prostatitis results in marked inflammation of part or all of the prostate gland. Numerous polymorphonuclear leukocytes are noted within and around the acini, along with intraductal desquamation and cellular debris, and varying degrees of tissue invasion by lymphocytes, plasma cells, and macrophages. Diffuse edema and hyperemia of the stroma are seen. Micro-abscesses may occur early; large abscesses are late complications.

The histologic features of chronic bacterial prostatitis are non-specific. The inflammatory reaction is, in general, much less marked than that of acute bacterial prostatitis. Intraacinar and periacinar round cell infiltration and varying degrees of invasion by plasma cells and macrophages are noted histologically. Since these changes are frequently seen in specimens of patients who have no history or laboratory evidence of bacterial infection involving the genitourinary tract, they are not diagnosed of bacterial prostatitis (Bourne and Frishette, 1967).

Clinical Manifestations.—Acute bacterial prostatitis is characterised by fever, chills, perineal and low back pain, dysuria, urinary frequency and urgency, and varying degrees of obstructive symptoms. A warm, exquisitely tender prostate gland, which is usually swollen, irregular, and indurated, is found on physical examination.

Chronic bacterial prostatitis is variable in manifestation. Many patients present with asymptomatic bacilluria, normal prostate glands by rectal palpation, normal excretory urograms, and no residual urine. Most patients experience irritative voiding symptoms, with or without back pain, low grade fever, and myalgia or arthralgia. Unless prostatic hypertrophy is also present, their excretory urograms are also normal. These patients respond readily to sterilization of the urine with appropriate antibiotics; however, relapse of symptoms and reinfection of the bladder urine usually follow withdrawal of drug therapy. In calculous prostatitis the bacterial pathogen may actually become embedded within the stones and serve as a nidus for perpetuating the infection. Other signs of prostatitis include urethral discharge, hemospermia (occasionally), and secondary epididymo-orchitis.

Diagnostic Parameters.—Because the clinical picture and physical findings are quite characteristic, acute bacterial prostatitis is usually recognised by the physician. Large numbers of bacterial pathogens grow on culture plates of the expressed prostatic secretions. Massage of acutely inflamed prostate glands, however, may result in bacteremia and should never be done unless appropriate antibiotic therapy has already been started. Since cystitis usually accompanies acute bacterial prostatitis, the pathogen is often readily identified by culture of the voided urine.

Chronic bacterial prostatitis is a bacteriologic diagnosis: the medical history, physical examination, X-ray studies, and cystoscopic examination are not specifically diagnostic. That one cannot make a diagnosis of chronic bacterial prostatitis from the number of leukocytes in the expressed prostatic secretion is well-documented (O'Shaughnessy *et al.*, 1956; Bowers and Thomas, 1958; Bourne and Frishette, 1967). Tissue culture of prostatic needle biopsy specimens is likewise ineffective for diagnosis (Schmidt and Patterson, 1966). Since the infection is usually focal, and since such specimens are random, small, and easily contaminated during procurement, the low yield of valid cultures with this technique is easily understood. Because conditions other than bacterial infection produce similar changes, the histologic presence of chronic inflammation is not diagnostic of chronic bacterial prostatitis (Bourne and Frishette, 1967).

The diagnosis of bacterial prostatitis is substantiated in the laboratory when quantitative bacteriologic techniques clearly localise pathogenic bacteria to the prostate gland. Chronic bacterial prostatitis is often characterised by the growth of small numbers of bacteria on culture plates of prostatic fluid (Meares and Stamey, 1968). Since urethral organisms of non-prostatic origin can easily contaminate the prostatic fluid expressed by massage, isolated culture of the prostatic secretion is misleading. For diagnostic accuracy, the physician must obtain simultaneous quantitative cultures of the urethra, midstream urine, and expressed prostatic secretion. Careful collection of the segmented specimens and exacting culture techniques are both essential for proper diagnosis. Many laboratories do not report bacterial colony counts of 1,000 per ml. or less. Furthermore, when culture plates are surface-streaked with only a loop of specimen (total volume of 0·01 ml.), the culture may fail to grow organism despite the presence of 99 bacteria per ml. of specimen. Such laboratory techniques compromise the physician's ability to localise the prostatic infection.

Localisation Methodology.—The voided urine and expressed prostatic secretion are partitioned into segments: the first voided 10 ml. (VB1, the symbol for " voided bladder 1 "); the midstream aliquot (VB2, the symbol for " voided bladder 2 "); the pure prostatic secretion, expressed by massage (EPS, the symbol for " expressed prostatic secretion "); and the first voided 10 ml. immediately after prostatic massage (VB3, the symbol for " voided bladder 3 ").

To ensure proper collections the patient should be well hydrated and have a bladder that is full. If the patient is circumcised, cleaning of the glans is usually unnecessary. The uncircumcised man should be instructed to retract his foreskin and maintain this state throughout all collections. The glans is then cleaned with detergent soap, all soap is removed with a wet sterile sponge, and the glans is carefully dried. Thy physician collects the VB1 by holding the sterile culture tube directly in front of the meatus as the patient initiates voiding. As the patient continues to void, the physician quickly removes the culture tube from the stream of urine and waits until the patient has voided about 200 ml. At this point the VB2 culture tube is inserted into the stream of urine for collection of the 10 ml. mid-stream aliquot. The patient is then instructed to stop voiding. Securely retracting the foreskin, the patient then bends forward. During prostatic massage the physician collects drops of prostatic fluid directly into a wide mouth sterile container, which he holds directly in front of the meatus. Collection of this fluid is facilitated by gentle pressure on the bulbar urethra upon completion of the massage. Immediately after massage, the patient voids again and the VB3 is collected in similar fashion as the VB1. Even if the physician has been unable to collect drops of EPS, a clear VB1 and a cloudy VB3 specimen usually means that prostatic fluid is present in the VB3 specimen.

Interpretation of Data.—When the bladder urine is *sterile*, the physician can differentiate urethral and prostatic infection by comparing the bacterial colony counts of the urethral (VB1) and prostatic (EPS and VB3) cultures. In urethral infection, the VB1 count usually significantly exceeds the EPS or VB3 count. In prostatic infection, the EPS and VB3 count usually far exceed the VB1 count. When sufficient EPS cannot be obtained for direct culture, one must remember that the VB3 specimen is about a 100-fold dilution of prostatic fluid. After prostatic massage, only about 0·1 ml. of prostatic fluid remains along the urethra. When this 0·1 ml. of prostatic fluid is then collected in 10 ml. of sterile bladder urine, it is diluted 100-fold. In bacterial prostatitis, therefore, the bacterial colony count of the EPS culture always exceeds that of the VB3

TABLE

Date	Patient	Days On (+) or Off (−) Drug	Bacteria per ml.				Organism
			VB1	VB2	EPS	VB3	
8.2.66	E. S.	−9 Pen. G.	100,000	100,000	—	100,000	*E. coli*
10.3.66	E. S.	−5 Amp.	0	0	—	50	*E. coli*
11.3.66	E. S.	−6 Amp.	10,000	10,000	—	10,000	*E. coli*
14.3.66	E. S.	+3 Amp.	0	0	—	50	*E. coli*
22.3.66	E. S.	−6 Amp.	100,000	100,000	—	100,000	*E. coli*
1.4.66	E. S.	+9 Nitrofur.	0	0	—	300	*E. coli*
18.4.66	E. S.	−6 Amp.	100,000	100,000	—	100,000	*E. coli*
20.4.66	E. S.	+1 Colistin	0	0	—	1,250	*E. coli*
4.5.66	E. S.	−10 Colistin	8,000	8,000	—	10,000	*E. coli*
28.7.66	S. T.	1st Infection	100,000	100,000	—	100,000	*E. coli*
18.8.66	S. T.	−10 Pen. G.	0	0	120	0	*E. coli*
25.8.66	S. T.	−17 Pen. G.	0	0	10,000	600	*E. coli*
20.10.66	S. T.	−31 Nal. Acid	100,000	100,000	100,000	100,000	*E. coli*
22.12.66	S. T.	+21 Amp.	0	0	1,500	120	*E. coli*
12.1.67	S. T.	−7 Amp.	0	0	4,000	120	*E. coli*
23.1.67	S. T.	−18 Amp.	100,000	100,000	100,000	100,000	*E. coli*
11.9.67	T. L.	−43 Nal. Acid	—	100,000	—	—	*E. coli*
14.9.67	T. L.	+4 Amp.	10	0	1,300	40	*E. coli*
17.9.67	T. L.	+6 Amp.	10	0	1,900	30	*E. coli*
23.4.69	T. L.	+23 Nitrofur.	0	0	410	70	*E. coli*
19.4.65	J. T.	1st Infection	—	100,000	—	—	*Kleb.*
11.9.67	J. T.	+3 Nitrofur.	50	0	100,000	—	*Kleb.*
16.10.67	J. T.	+35 Nal. Acid	10	0	10,000	—	*Kleb.*
14.2.68	J. T.	−90 Kanamycin	0	0	10,000	—	*Kleb.*
24.9.68	J. T.	+210 Nal. Acid	2,500	1,000	100,000	3,000	*Kleb.*

Legend: VBI = first voided 10 ml. of urine (urethral culture); VB2 = midstream aliquot (bladder culture); EPS = expressed prostatic secretion (prostatic culture); VB3 = first voided 10 ml. of urine after prostatic massage (prostatic culture). Pen. G. = penicillin G; Amp. = ampicillin; Nitrofur. = nitrofurantoin; Colistin = sodium sulfamethyl colistin; Nal. Acid = nalidixic acid. *El coli* = *Escherichia coli*; *Kleb.* = *Klebsiella* species.

culture. When the VB1 and VB3 colony counts are small and similar, the EPS culture is particularly useful in localisation of the infection.

When the bladder urine is *infected*, these techniques cannot be initially used to localise the infection because all specimens will generally show heavy growth of organisms. Instead, therapy with an appropriate antibiotic should be initiated. After 2 or 3 days of drug therapy, the segmented specimens are then obtained for localisation of the infection. Despite the presence of bactericidal drug levels in the urine, and sterile VB1 and VB2 specimens, the VB3 and EPS specimens of patients who have chronic bacterial prostatitis usually grow the pathogen on surface-streaked culture plates. To prevent false negative results, however, EPS and VB3 specimens that are obtained during drug therapy must be immediately refrigerated or surface-streaked immediately on to culture plates. In our experience the antibiotic will diffuse into the media and the bacteria will still grow on the surface of the culture plate. When the VB1 and VB2 cultures are sterile, positive EPS and VB3 cultures are unequivocally diagnostic of bacterial prostatitis.

Clinical examples of the localisation of chronic bacterial prostatitis are illustrated in the Table. Diagnostic reliability has been confirmed by the uniform reproducibility of culture patterns in patients who have had numerous cultures throughout months or years of treatment.

Therapy.—Patients who have acute bacterial prostatitis often respond dramatically to antibiotic therapy. Selected by susceptibility testing of the pathogen, an antibiotic should be given in sufficient dosage to assure bactericidal levels of the drug in the plasma. Supportive measures, such as adequate hydration, analgesics, antipyretics, and stool softeners are also employed.

Antibiotics rarely, if ever, cure chronic bacterial prostatitis. Despite therapy with a variety of antibiotics, most patients show persistence of the pathogen in prostatic fluid cultures. Reinfection of the bladder urine and recurrence of symptoms generally occur within a few days of drug withdrawal.

Animal research has clearly shown that various antibacterial agents useful *in vitro* against gram-negative pathogens do not diffuse across intact prostatic epithelium in sufficient concentration to kill the pathogen *in vivo* (Dunn and Stamey, 1967; Winningham *et al.*, 1968; Stamey *et al.*, 1970; Winningham and Stamey, 1970). The principles that govern drug diffusion from plasma into prostatic fluid have been previously reported (Winningham *et al.*, 1968; Stamey *et al.*, 1970). Although the relatively new bactericidal agent, trimethoprim, achieves bactericidal concentrations in canine prostatic fluid (Reeves and Ghilchik, 1970; Robb *et al.*, 1971), we have several treatment failures with standard dosage of trimethoprim-sulfamethoxazole for a total of 2 weeks' therapy in patients who have chronic bacterial prostatitis (unpublished observations). Because trimethoprim fulfils most of the theoretical criteria for diffusion into prostatic fluid, perhaps a longer treatment period would result in more cures of chronic bacterial prostatitis.

Since patients who have acute bacterial prostatitis seem to respond to antibiotic therapy, we assume that the intense inflammatory reaction somehow permits the transfer of drugs across the normally impermeable prostatic epithelium.

Total prostatectomy offers the most definitive cure of chronic bacterial prostatitis. The potential complications of such surgery, however, severely limits its applicability to benign disease. Transurethral prostatectomy is curative when all infected tissue is removed. Few of our patients who have had transurethral resections for chronic bacterial prostatitis have actually been cured. Of those who were not cured, however, none was made worse. Each simply resumed his previous pattern of recurrent bladder infections and persistently positive prostatic fluid cultures with the same pathogen. Most of our patients with this disease defer surgery and remain relatively asymptomatic during continuous, suppressive antibiotic therapy. Despite months of continuous therapy and sterile bladder urine, the pathogen persists in prostatic fluid cultures. Discontinuation of antibiotic therapy eventually results in reinfection of the urine and recurrence of symptoms.

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ANALYSES OF THE URETHRAL PRESSURE PROFILE BY MEANS OF ELECTROMYOGRAPHY AND THE ADMINISTRATION OF DRUGS

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The investigations concerning the urethral resistance can be divided into three groups:

1. Investigations which determine the total urethral resistance by means of pressure- and flow-studies (Ritter, Zinner and Paquin 1964; Smith, Edwards and Bryant, 1966; Smith, 1968; Gleason and Lattimer, 1962; Gleason, Bottaccini, Perling and Lattimer, 1967; Ritter, Sterling and Zinner, 1970; Kleeman, 1966).
2. Investigations in order to examine the pressure relations in the lumen of the urethra during micturation (Zinner and Ritter, 1967).
3. Investigations concerning the wall tension of the urethra at rest. This can be done by means of an open catheter with constant flow (Brown and Wickham, 1969) or by registration of the wall pressure by means of one or more balloons (Enhörning, 1961; Enhörning, Miller and Hinman, 1964).

The first method gives no information about the site where the resistance in the urethra is highest. The second method can indicate where during micturation the resistance in the urethra is at its highest level. However, during micturation there is a relaxation of the muscle elements in the urethra, so that no information is obtained about the tonus of these elements at rest. The third method does supply an insight into this. It was our purpose to determine:

(i) at which site in the urethra the wall tension is highest, and
(ii) by which structures (smooth muscles, striated muscles, blood-vessels or elastic tissue) this tension is brought about.

There appears to be no consensus of opinion about the rôle of the striated muscles in this area. Cass and Hinman (1968), in their experiments on dogs, did not find any influence from the striated muscles on urethral resistance, whereas Tanagho, Meyers and Smith (1969b) conclude that striated muscle contributes to over 50 per cent of the static urethral resistance. Dortermann and Bauer (1955), and also Lapides *et al.* (1957), after elimination of the activity of the striated muscles by means of muscle-relaxant drugs, observed no incontinence; the tonus of the urethra in the area of the sphincter externus remained the same. While there are conflicting views about the influence of the striated muscles on the wall tension, opinions about the innervation of the smooth muscle components also disagree. Whereas Tanagho, Meyers and Smith (1969a) consider the smooth muscles of the urethra to be completely innervated by the parasympathicus, Kleeman (1970), however, ascribed an important influence to sympathetic innervation. The examinations described here were carried out in order to obtain more elucidation about this subject.

Material.—The investigations were performed mainly in adult men and women (aged 18-63) with normal micturation, without incontinence or neurological diseases. By way of exception (see A III), to assess the influence of the striated muscles on urethral pressure, 3 patients with neurological disturbance were examined. In preliminary experiments, the normal pressure profile in the urethra was determined in 12 adult women and 5 adult men. The results are briefly summed up. In the further described investigations, carried out in order to analyse which wall structures determine the tension profile, the following observations were performed.

A. Influence of the striated urethra-musculature

I. In 21 normal men and women the urethral pressure profile and the electrical activity of the striated musculature of the urethra were investigated.

II. In 3 normal women the activity of the striated muscles of the urethra was eliminated by means of suxamethonium chloride, without applying general anæsthesia.

III. In 3 patients with paralysed striated musculature in neurological diseases the urethral pressure profile was determined.

B. Influence of the smooth musculature and autonomous innervation

IV. In 8 normal women the influence of parasympatholytics and in 6 normal women the influence of parasympathomimetics on the wall tension profile was examined.

V. In 6 normal women the influence of α-adrenergic blockade and administration of catecholamines was investigated.

VI. In 6 normal women the influence on the pressure profile of angiotensin and catecholamine was compared after paralysis by α-adrenergic blockade.

Method.

(a) *Pressure measurement in the urethra*

We determined the wall tension profile of the urethra by slowly withdrawing a water-filled balloon catheter from the bladder through the urethra.

Through a thin catheter with a $\frac{1}{2}$ cm. scale the pressure changes inside the balloon were transmitted to a transducer (Stratham P 23) on a Sanborn or Gallileo amplifier and registered on paper which runs with a velocity of 2·5 mm./sec.

The following experimental conditions were complied with:

1. The experimental subject was examined in a supine position;
2. The bladder had been emptied;
3. The length of the urethra was measured before with a calibrated 12 Fr. Foley-balloon catheter;
4. For determining the urethral pressure profile in adults we used a balloon of 5 mm. diameter;
5. The balloon was filled to a pressure of 30-35 mm. Hg, after being introduced into the bladder;
6. The balloon being in the bladder, the pressure measured there was considered as 0-line;
7. The curves obtained were measured.

(b) *Electromyography of the urethra and the pelvic floor musculature*

The electromyographic examination was performed simultaneously with determination of the pressure profile in the recumbent experimental subject with empty bladder. In women localisation of the sphincter externa urethræ was made by introducing the needle electrode 0·5 to 1 cm. lateral to the externus urinary meatus, 1 to 3 cm. deep, running parallel to the urethra. The electrodes were implanted under digital vaginal control. In men the electrode was placed 1 cm. behind the bulbus urethræ in the median line 2·5 to 4 cm. deep under digital rectal control. For the accuracy of sphincter externus localisation, we used the sound amplifier or the screen of the cathodic oscilloscope. The highest activity shown by either is the best indication that the tip of the needle is inserted in the sphincter. The amplification and registration were performed with a Sanborn S.350 amplifier and recorder.

(c) The drugs administered were:

(i) Parasympatholytic: atropine sulphate $\frac{1}{2}$ mg. intravenously;

(ii) Parasympathomimetic: carbachol $\frac{1}{4}$ mg. intramuscularly;

(iii) Sympatholytic: 10-20 mg. phentolamine (Regitine, CIBA) intravenously;
(iv) Sympathomimetic: 3-5 mg. metaraminol bitartrate (Aramine, Merck, Sharp & Dohme), intravenously;
(v) Vasoconstricting drugs: angiotensin (Hypertensine, CIBA), 15 μg. intravenously;
(vi) Striated muscle paralysing drug: suxamethonium chloride (Scoline, Allen & Hanbury Ltd.), 75-150 mg. intravenously. This drug was administered to experimental subjects who were on the point of undergoing an operation, but before being anæsthetised.

They were informed about the symptoms of paralysis which would occur. Respiration was ensured by means of a respirator. Pain-killing proved unnecessary.

The investigations were done in men as well as women. Comparable observations at each point of the urethra could be made only in women, since the length of the urethra did not change during the investigation. In men the urethra nearly always lengthened, so that the determination of position, made from the meatus externus, was not exact during the examination.

The tension in the wall of the urethra was measured from every 5 to 5 mm.

The observations in different experimental subjects with naturally different urethral lengths were reduced to the value of each one-fifth part of the urethral length. In this way the values of all identical fifth parts could be compared and the average could be calculated.

Results.—*Preliminary studies*:—

In preliminary studies in 12 adult women and 6 adult men without micturation disturbances the normal shape of the urethral pressure profile was investigated. It appeared that:

1. In women the average length of the urethra was 4·1 cm. (3·5-5 cm.), the point of the highest wall tension was 1.8 cm. from the bladder outlet, with a variation of 1-2·5 cm.

   An area with an average length of 2·8 cm. showed a higher pressure than was measured in the bladder (variation 2-3·5 cm.). The last cm. of the urethra showed a pressure identical to or lower than that in the bladder. In 6 adult men the point of the highest pressure was situated at 4 cm. from the bladder outlet.
2. The pressures in the urethra measured with balloons of 3, 4, 5, 6 and 7 mm. diameter were directly proportional to the diameter of the balloons. On the ground of the results obtained, the procedure in adults was standardised by using balloons with a diameter of 5 mm.
3. There was no difference in the shape of the curve in the case of either an empty or a full bladder when there was no micturation urgency. At the appearance of micturation urgency a lowering of the profile was observed.
4. There was no difference in pressure profile either in lying or in standing position.

In women the average highest pressure was 50 mm. Hg (18-67 mm. Hg), in men it was 69 mm. Hg (37-138 mm. Hg).

A. Influence of the Striated Musculature on the Urethral Pressure Profile

I. Simultaneous registration of the urethral pressure profile and the E.M.G. of the striated musculature of the urethra was performed in 21 individuals. In 12 of them no enhanced activity of the striated musculature was observed while the balloon was passed through the urethra; in 4 of them there was only little reaction.

In 5 individuals a marked activity was observed when passing the balloon through the urethra. They showed no significantly raised pressure profile (Fig. 1).

From these data it appears that the highest part of the curve of the urethral pressure profile is not induced by active contraction of the striated musculature.

In men the urethral pressure profile is changed only by active contraction of the striated musculature (" hold urine "), distal from the site of the highest tension (Fig. 2

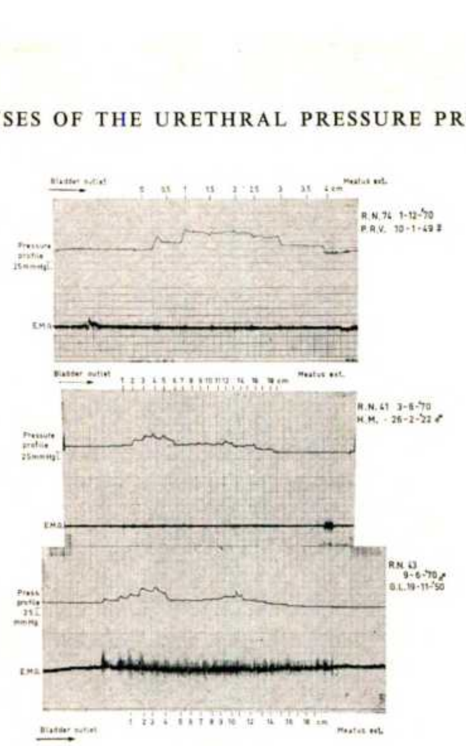

FIG. 1

Urethral wall tension profile simultaneously with electromyography of the external sphincter.
RN 74 Woman with urethra of 4 cm. length. On passing the balloon there is a slight activity of the striated muscles.
RN 41 Man with hardly any activity of the striated muscles but with a normal profile.
RN 43 Man with high activity of the striated muscles with a normal profile.

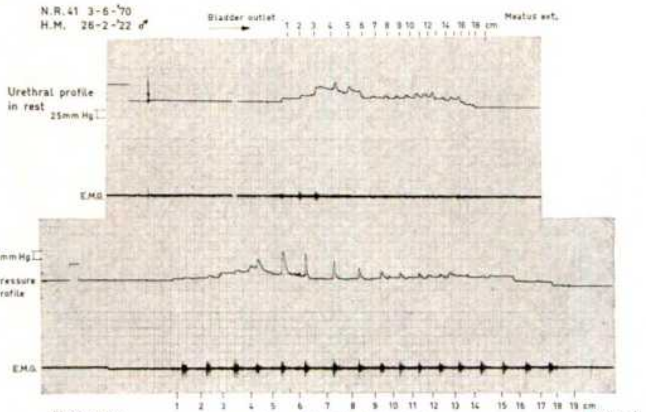

FIG. 2

The top curve shows the pressure profile and E.M.G. in rest. The lower curve shows the pressure changes in the urethra with empty bladder when the subject contracts the striated muscles. The greatest influence of active contraction on the tension profile is seen after the balloon has passed the top of the tension profile.

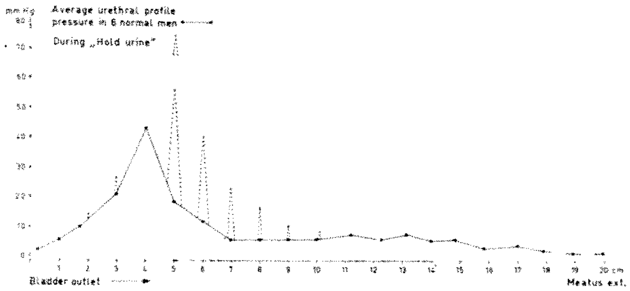

FIG. 3

The average value of the urethral wall tension profile in 6 normal men, with the average elevation of tension during active contraction of the striated pelvic floor muscles.

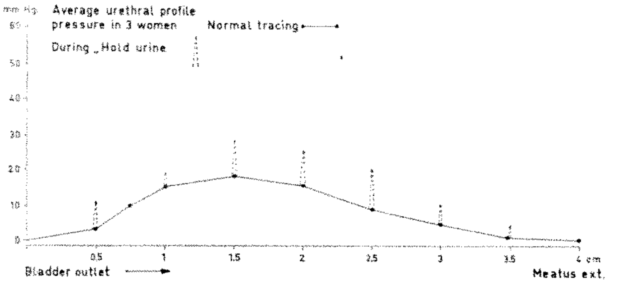

FIG. 4

The average value of the urethral tension profile in 3 normal women. The elevation of the tension caused by active contraction of the pelvic floor muscles is superimposed.

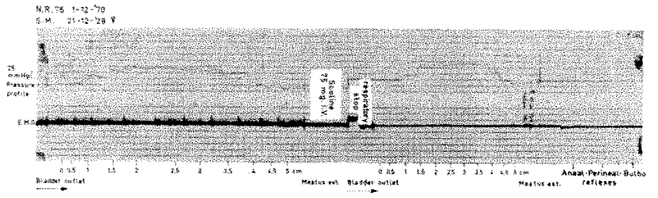

FIG. 5

Urethral wall tension profile simultaneously with E.M.G. Urethral length 5 cm. First without muscle relaxant. Balloon slowly passed the urethra. Mid-urethra pressure 70 mm. Hg. On passing the balloon there is some more activity of the striated muscles. After administering 75 mg. succinylcholine, all electrical activity of the striated muscles stopped, also the reflexes disappeared. The tension profile is only slightly changed.

and Fig. 3). In women (Fig. 4) the pressure rise during active contraction does occur at the highest point of the curve and distal from it.

II. In 3 normal women the striated musculature was paralysed after intravenous administration of 100-150 mg. scoline without anæsthesia. The electrical activity of the striated urethral-musculature was examined by means of electromyography before and after administration of the muscle relaxant, simultaneously with determination of the pressure profile.

The pressure profile hardly changed (Fig. 5). The average values of the determination in 3 normal women are shown in Table I and Figure 6. The tension in the middle part of the urethra remains almost the same. Only the second fifth part is lowered.

TABLE I

Urethral Pressure in 3 Normal Women without Drugs and after 100-150 mg. succinylcholine (i.v.) without General Anæsthesia

Distance from Bladder Outlet	1/5		2/5		3/5		4/5		5/5	
100-150 mg. succinylcholine i.v.	mm. Hg −	+	mm. Hg −	+	mm. Hg −	+	mm. Hg −	+	mm. Hg −	+
Patient 1	30	20	70	50	60	60	25	15	0	0
2	20	5	45	30	60	50	15	20	−5	0
3	5	5	40	10	55	40	40	45	0	5
Average	18	10	52	30	58	50	27	27	−2	+2

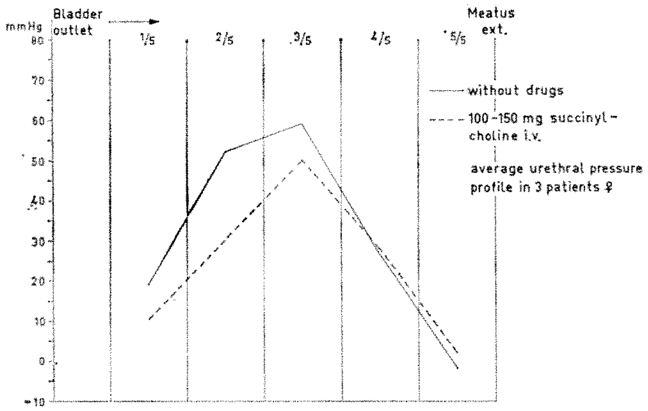

FIG. 6

The average value of the tension profile in 3 normal women, before and after 100-150 mg. succinylcholine intravenously.

III. One patient (Fig. 7) without any activity of the striated pelvic floor muscles and also without any reflex activity (A) proved to have a normal pressure profile (60 mm. Hg) covering 2 cm. urethra length (B). Another patient (Fig. 8), a man with myelodysplasia through spina bifida, who did not show any electrical activity of the striated muscles, nor any reflex activity (A), had a normal high pressure profile (75 mm. Hg, B). A third patient, who underwent a bilateral pudendal neurectomy, so that there was no electrical activity of the striated muscles, had a normal pressure profile.

From these observations (I, II and III) we can conclude that the shape of the urethral pressure under the afore mentioned conditions is not determined by the activity of the striated muscle tissue, connected with the posterior urethra.

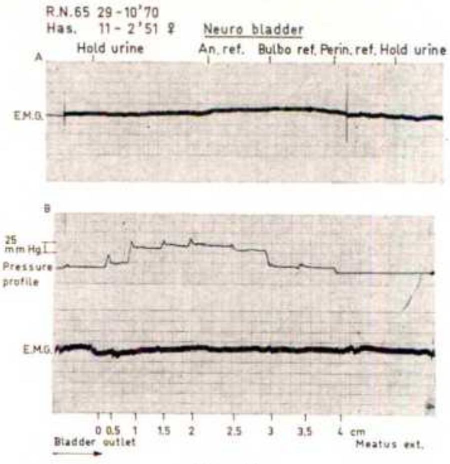

FIG. 7

Woman (19 years old) with tumor cauda equina and paralysis of the pelvic floor without any reflex activity. There is a normal pressure profile.

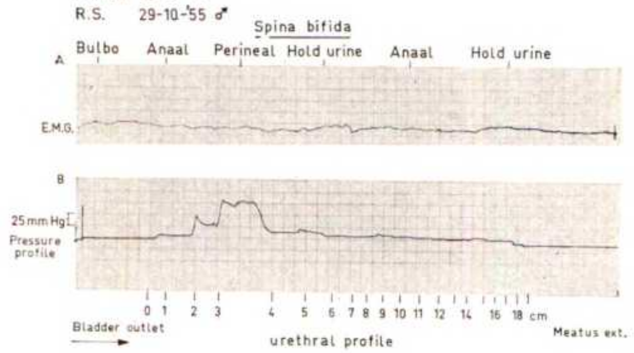

FIG. 8

Man (14 years old) with spina bifida and paralysed pelvic floor, without reflex activity and without ability of active contraction, had a high pressure profile (highest level at 3-4 cm. from the bladder neck).

B. Influence of the Smooth Musculature

IV. *The action of anticholinergic and cholinergic drugs*

In 8 women the wall tension was determined before and 3-8 minutes after intravenous administration of $\frac{1}{2}$ mg. atropine sulphate. No influence was observed on the pressure profile (Table II, Fig. 9).

Administration of a parasympathomimetic drug did not yield any significant changes of the profile either.

Table III and Figure 10 shows the average values in 6 women before and 5-10 minutes after intramuscular administration of $\frac{1}{4}$ mg. carbachol, from which no effect was observed.

V. *The action of anti-adrenergic and adrenergic drugs*

The influence of phentolamine (Regitine) an α-receptor blocking-agent, and the action

TABLE II

Urethral Pressure in 8 Normal Women without Drugs and
3 to 8 min. after ½ mg. atropine i.v.

Distance from Bladder Outlet	1/5		2/5		3/5		4/5		5/5	
	mm. Hg		mm. Hg		mm. Hg		mm. Hg		mm. Hg	
½ mg. atropine i.v.	−	+	−	+	−	+	−	+	−	+
Patient 1	15	0	15	15	25	25	10	10	−10	−10
2	5	5	40	35	45	45	30	15	0	−5
3	15	20	30	50	60	60	25	20	0	0
4	5	0	40	45	75	65	30	55	−5	5
5	30	30	55	55	60	55	10	15	−5	−5
6	15	15	80	85	65	55	40	30	−5	−5
7	15	20	25	30	20	30	5	15	−5	−5
8	20	20	60	50	10	30	5	5	−5	+5
Average	15	14	43	46	45	46	20	21	−4·5	−2·4

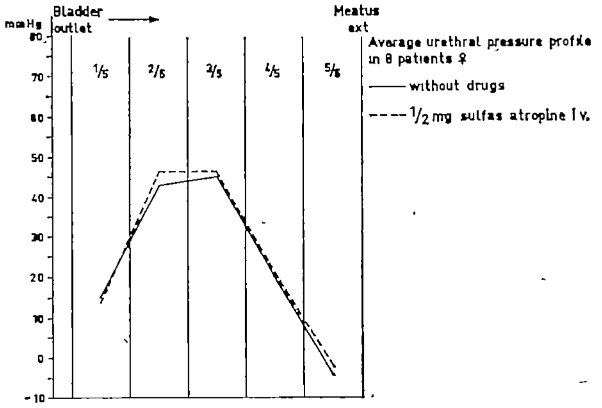

FIG. 9
The average values of Table II are visualised in this figure.

of Aramine, an adrenergic drug (metaraminol bitartrate), administered afterwards, were studied in 6 normal women. After blocking totally or partially the adrenergic receptors (10 mg. Regitine i.v.), the wall tension in the entire urethra sharply decreases. The decrease is most pronounced in the middle part of the urethra and occurs after 1-3 minutes. If, after 10 minutes, 3-5 mg. Aramine is administered intravenously, the wall tension recovers to almost the original values (Table IV, Fig. 11). There is an evident influence of sympatholytic and sympathomimetic drugs on the urethral pressure profile.

VI. The above-described influence of the adrenergic system can affect the smooth musculature of the urethra or the blood-vessels which are so abundant in the urethral wall.

The blood pressure can serve as a parameter for the action of phentolamine (Regitine) on the peripheral vessels. In all our observations the blood pressure did not significantly decrease after intravenous administration of 10 mg. Regitine; however, tachycardia revealed itself. Table V and Figure 12 also show that the average value of the blood pressure in 6 normal women after administration of 10 or 20 mg. Regitine did not decrease. On account of this it seems improbable that the decrease of the urethral pressure profile should be caused by the calibre change of peripheral vessels in the urethral wall. The rise of the profile to almost normal values by the administration of

TABLE III

Urethral Pressure in 6 Normal Women without Drugs and 5 min. after ¼ mgr. carbachol (i.m.)

Distance from Bladder Outlet	1/5		2/5		3/5		4/5		5/5	
¼ mg. carbachol i. v.	mm. Hg –	 +	mm. Hg –	 +	mm. Hg –	 +	mm. Hg –	 +	mm. Hg –	 –
Patient 1	5	5	20	25	35	30	15	15	–10	–10
2	5	5	15	20	40	40	25	25	0	0
3	20	25	45	55	45	45	20	20	0	0
4	5	5	40	25	45	45	25	15	0	–5
5	5	10	45	70	60	60	15	5	0	0
6	5	10	20	30	75	70	15	10	0	0
Average	7·5	10	31	37·5	50	48	19	15	–2	–2·5

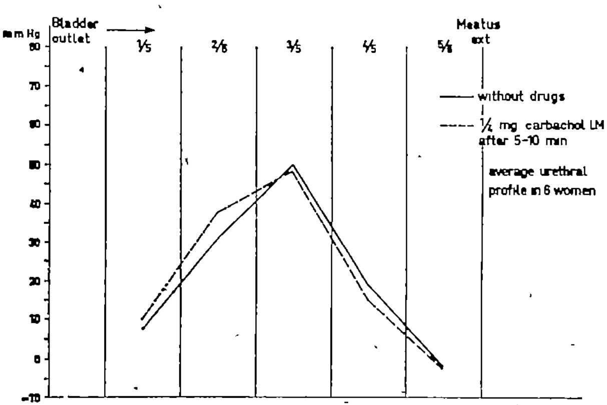

FIG. 10
The average values of Table III are visualised in this figure.

TABLE IV

Urethral Pressure in 6 Normal Women without Drugs and 3 to 6 min. after 10 mg. phentolamine (i.v.) followed by 3-5 mg. metaraminol (i.v.)

Distance from Bladder Outlet	1/5			2/5			3/5			4/5			5/5		
10 g. phentolamine 3-5 mg. metaraminol	—	mm. Hg phento.	metar.	—	mm. Hg phento.	metar.	—	mm. Hg phento.	metar.	—	mm. Hg phento.	metar.	—	mm. Hg phento.	metar.
Patient 1	5	5	5	25	5	25	45	15	35	20	25	20	−5	−5	−5
2	5	5	0	5	5	25	40	10	45	20	5	5	0	0	0
3	20	5	10	35	15	20	55	20	35	25	10	10	0	0	0
4	5	2	5	25	10	25	75	25	75	25	15	15	5	5	−5
5	5	5	10	45	20	30	60	30	60	10	5	30	−5	−5	−5
6	5	5	5	20	20	45	75	25	60	30	15	35	0	0	0
Average	7·5	4·5	6	26	12·5	28	58	21	52	22	12·5	19	−1	−1	−2

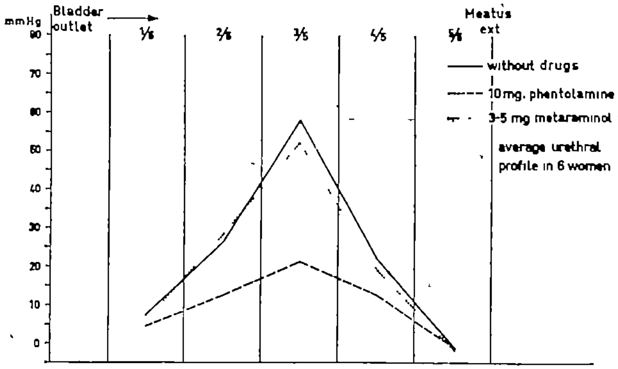

FIG. 11
The average values of Table IV are visualised in this figure.

TABLE V

Urethral Pressure in 6 Normal Women without drugs, after 10-20 mg. phentolamine, 15 μg. angiotensin and 3-5 mgr. metaraminol

Distance from Bladder Outlet	1/5				2/5				3/5				5/5				5/5							
10-20 mg. phentolamine 15 µg. angiotensine 3-5 mg. metaraminol	mm. Hg				mm. Hg.				mm. Hg				mm. Hg.				mm. Hg				Blood Pressure			
	—	phent.	ang.	meta	—	phent.	ang.	meta	—	phent.	ang.	meta	—	phent.	ang.	meta	—	phent.	ang.	meta	—	phent.	ang.	meta
Patient 1	5	5	5	0	20	5	10	20	55	25	30	50	45	15	25	30	−5	−5	−10	−5	130/70	130/70	190/110	200/100
2	25	15	15	15	70	55	55	65	70	40	45	55	55	35	15	40	10	0	0	0	130/80	130/80	180/100	200/110
3	5	5	0	0	30	15	10	25	25	15	10	25	5	0	5	15	0	−10	−10	−10	140/80	140/80	170/100	180/110
4	15	10	5	5	25	15	15	25	20	15	15	25	5	15	5	10	−5	0	−5	0	130/90	110/80	190/100	210/100
5	10	15	10	25	50	30	30	40	35	20	20	25	25	10	5	0	0	0	0	−5	160/160	180/100	210/130	220/110
6	10	10	15	10	25	25	25	30	35	30	35	40	25	25	20	20	0	0	0	0	130/80	120/80	180/100	200/100
Average	12	10	9	9	37	24	23	34	40	24	26	37	27	17	13	21	0	−3	−4	−3				

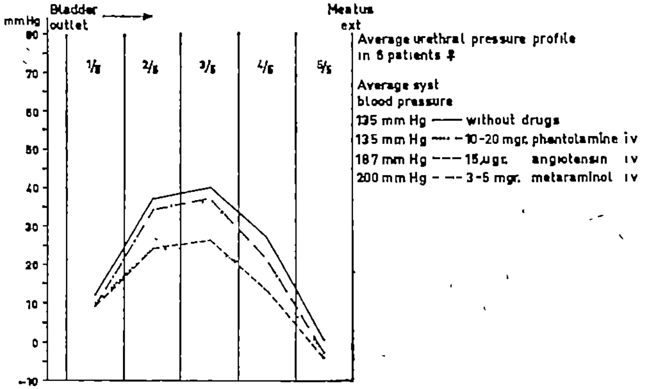

FIG. 12

The average values of Table V are visualised in this figure.

metaraminol is attended by a vigorous rise of the blood pressure (from an average of 135 to an average of 200 mm. Hg; Fig. 12).

In order to exclude that the rise in wall tension was caused by vessel activity after administration of phentolamine 15 μg antiotensin (Hypertensine, CIBA) was administered intravenously. This raised the blood pressure for 4-5 minutes, without exerting any influence on the wall tension in the urethra (Table V, Fig. 12). By this any influence on the diameter and tension or filling of the vessels in the urethra as the cause of the total wall tension change is rendered most unlikely.

If, however, 5 minutes after administration of angiotensin, the blood pressure had returned to normal again and metaraminol was administered intravenously, the blood pressure rose to an average of 200 mm. Hg, but at the same time the urethral pressure profile reverted to almost normal values.

DISCUSSION

Our observations by means of electromyography and the administration of drugs which influence the activity of striated and smooth muscles, were chiefly performed in normal individuals with an empty bladder and in the supine position. They give us no insight into the relations with the filled bladder and consequently no data about the factors which influence continence in normal and pathologic conditions.

According to our findings, the contribution of the striated muscles to the urethral pressure profile is very small, for the activity of the striated muscles contributed only insignificantly to the urethral pressure profile when the bladder was at rest. Changes caused by pharmacological or pathological paralysis, hardly affected the pressure profile.

Tanagho *et al.* (1969*b*) came to the conclusion that in dogs 50 per cent of the total urethral resistance was brought about by the striated muscles. By means of sphincterometry in individuals, Scultety and Arbandi (1960) found a slight reduction of 20 per cent of the original value after administration of Scoline.

Lapides *et al.* (1960) as well as Dortermann and Bauer (1955) observed no incontinence after administration of Scoline or *d*-tubocurarine. Obviously, there are quite a few contradictory concepts about the rôle of the striated muscles. In our observations it is conspicuous that the first two-fifth part of the urethra from the bladder indeed reveals a less raised pressure after administration of succinylcholine (see Fig. 2); in the third- and fourth-fifth part, however, where the majority of the striated muscles are situated, the wall tension remains almost constant after administration of suxamethonium chloride.

The increased wall tension in the urethra might be caused by:

(*a*) Vascular tissue.
(*b*) Smooth tissue.
(*c*) Elastic tissue.

The elastic tissue does not contribute to the urethral pressure profile for the following reasons:

1. According to anatomic observations (Woodburne, i.a. (1967)), most elastic tissue is situated at the bladder neck and first part of the urethra, while the pressure profile is highest in the middle of the urethra.
2. Sympatholytics and sympathomimetics do not affect the elastic fibres.

According to our observations it is plausible that the urethral pressure profile is determined by the tonus of adrenergically influenced smooth muscles.

The adrenergic blocking-agent phentolamine significantly decreased the urethral pressure (Figs. 11 and 12), whereas administration of the sympathomimetic drug metaraminol, about 10 minutes later, restored the normal pressure profile.

The dose of phentolamine was not so high that it completely blocked the α-adrenergic effects, for by subsequent administration of metaraminol the effect of phentolamine on the urethra could be compensated and was accompanied by a rising blood pressure. However, from the fact that a marked tachycardia occurred after phentolamine administration, it is clear that the dosage used was higher than threshold. Tachycardia without change of the average blood pressure is a well known effect of phentolamine (Goodman and Gilman, 1970). Hence it may be concluded that the fall in the pressure profile after phentolamine was due to α-adrenergic blockade, and the normalisation after metaraminol is a result of stimulation of α-receptors. Furthermore, the absence of effect of the strongly vaso-active agent angiotensin suggests that vascular effects in the vicinity of the urethral area are of no consequence for the urethral pressure profile. In conclusion, drug-induced pressure changes must be mediated by sympathetic receptors in the musculature of the urethra.

This means that we have to assume that in the area of the external sphincter there must be a considerable quantity of smooth muscle tissue. As early as 1954 Elliott came to this conclusion on the grounds of clinical observations. He demonstrated the presence of smooth muscle tissue at the apex of the prostrate, to which he ascribed an important rôle in the involuntary control of urine. Similar conclusions were drawn by Nemoy and Govan (1969) and by Krahn and Morales (1965). Anatomic and embryologic investigations carried out by Dröes (in press) and Van Ulden (in press) prove that the woman's urethra and the man's proximal urethra contain smooth muscle tissue, which bears no relation to the bladder and which has had its own development.

Our observations demonstrate that these muscle groups are influenced by the sympathetic nerves. This would agree with the results of the flow studies by Kleeman, who found a significant influence of sympatholytics and sympathomimetics on the urethral musculature. However, he thought this influence to be greatest near the bladder neck; in our opinion, the more distal parts of the urethra a little proximal to the external sphincter are innervated by the sympathetic nerves. In following publications we hope to illustrate this from clinical observations.

CONCLUSION

In experiments on individuals with normal micturation it was demonstrated by means of electromyography and drugs that:

1. The urethral pressure profile is mainly determined by the activity of smooth muscle tissue.
2. This smooth muscle tissue is innervated by sympathetic nerves.

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HEPATITIS AND EPIDEMIC HEPATITIS ASSOCIATED ANTIGEN (E.H.A.A.) IN A HÆMODIALYSIS UNIT WITH OBSERVATIONS ON HÆMOGLOBIN LEVELS

By J. C. Coleman,[1] J. B. Eastwood,[1] J. R. Curtis,[1] R. A. Fox[2] and M. S. Edwards,[1]

There have been several reports of hepatitis in hæmodialysis units. In some the disease has been thought to be infectious hepatitis (Eastwood *et al.*, 1968) and in other outbreaks serum hepatitis (Friedman and Thomson, 1966). The description of Australia antigen (Blumberg *et al.*, 1965) and its subsequent correlation with serum hepatitis (Blumberg *et al.*, 1970; Prince *et al.*, 1970) enables some distinction to be made between the types of hepatitis occurring in hæmodialysis units. Since detection of Australia antigen has been possible, it has been found that many of the outbreaks in hæmodialysis units have been associated with this antigen.

In addition, Del Prete *et al.* (1970) have demonstrated recently an antigen associated with the disease pattern of infectious hepatitis which they refer to as epidemic hepatitis associated antigen (E.H.A.A.).

We describe an outbreak of hepatitis in a hæmodialysis unit in which E.H.A.A. was detected in two patients with hepatitis. Australia antigen (H.A.A.) was not detected in any patient with hepatitis. H.A.A. (Australia antigen) was detected on one occasion only in a patient with no symptoms and no biochemical evidence of hepatitis.

Kolk-Vegter *et al.* (1971) have reported rises in hæmoglobin levels in patients on regular hæmodialysis when they develop serum hepatitis. We describe significant rises in hæmoglobin levels during hepatitis in 9 patients in the present report.

The Hæmodialysis Unit.—The maintenance hæmodialysis unit at Fulham Hospital has been in operation since March 1964. Dialyses are carried out on six nights a week, each patient being dialysed twice weekly for a total of 28 to 32 hours. A single pass warm dialysis system using modified 2 layer kiil dialysers is employed. After each dialysis, the polypropylene boards of the dialysers are washed in Hæmosol (Meinecke and Co. Inc.), rinsed in tap water and reassembled using new cuprophane (PT 150) membranes. The membranes are prepared by soaking in a pan containing 2 per cent formalin (0·8 per cent formaldehyde) in pyrogen free water. Both the blood and dialysate compartments of the dialysers are filled with 2 per cent formalin (0·8 per cent formaldehyde) and left for 2 to 3 days. Immediately before the next dialysis, the formalin is drained away and the dialysate compartment is washed through with tap water. The blood compartment is washed through with normal saline and primed with heparinised normal saline.

Since November 1968, it has been the policy to restrict each patient to his or her own dialyser where possible. Dialysis fluid is distributed from a central supply. In February 1967, a tank system was abandoned in favour of a central proportioning system. After each dialysis, the supply system is rinsed with water and disinfected with 6 per cent formalin (2·4 per cent formaldehyde) for 1 hour. At week-ends, the formalin remains in the system for 24 hours.

Since August 1967, there has been a home dialysis programme and 2 to 3 of the 11 beds in the unit have been set aside for home training purposes. These patients use individual single patient proportioning machines. Some of these machines are disinfected by heat instead of formalin.

In October 1968, a renal transplantation programme was started.

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Arteriovenous Shunts.—Until August 1968, access to the circulation was gained exclusively by means of indwelling Teflon-silastic arteriovenous shunts. Since then subcutaneous arteriovenous fistula have been used in a number of patients.

Prophylaxis Against Hepatitis.—Prophylactic immunoglobulin in a dose of 750 mg. i.m.i. every 3 months has been given to all patients and offered to all staff since May 1966.

Since August 1966, during an earlier outbreak of hepatitis (1), gloves have been worn by nurses during " putting on " and " taking off " procedures. At the same time disposable crockery and cutlery were introduced and there was segregation of staff and patients for toilet arrangements. It was not until October 1970 that the staff ceased eating meals in the dialysis unit because there had been no practicable alternative.

Since July 1969 all prospective new patients have been screened for the presence of Australia antigen (H.A.A.) and would have been excluded had it been detected. Where possible, all blood for transfusion is also screened for H.A.A. (Australia antigen).

Each patient has his own dialyser, but single patient proportioning machines for home dialysis training may be shared between the same 2 or 3 patients. Since December 1970, in order to avoid contamination by blood of the " venous pressure " gauges in the patient monitoring equipment, a particularly long (2 metres) length of tubing is used between the gauge and the bubble trap of the venous blood line.

We strongly discourage " holiday " dialyses both by our patients in other units and by other patients in our unit. Prior H.A.A. (Australia antigen) screening would be mandatory before any such dialysis.

Criteria for the Diagnosis of Hepatitis.—Hepatitis was diagnosed when the serum glutamic oxaloacetic transaminase (S.G.O.T.) on a predialysis blood sample exceeded 40 Reitman Frankel units/ml. or when the serum glutamic pyruvic transaminase (S.G.P.T.) exceeded 35 Reitman Frankel units/ml.

Laboratory Surveillance.—Estimations of S.G.O.T., S.G.P.T. serum bilirubin and alkaline phospatase are carried out at least once a month on all hospital dialysis patients. When abnormalities are detected, these estimations are repeated weekly. On home dialysis patients, these estimations have been done at 1 to 3 monthly intervals.

In any patient or member of staff who develops a fever or becomes unwell in any way, liver-function tests are carried out urgently together with routine blood counts and screening for H.A.A. (Australia antigen).

Paul Bunnell Screening Tests have been carried out in patients with hepatitis. In a number of patients with hepatitis, screening for infection by toxoplasmosis and cytomegalovirus has also been done.

In a number of patients on long term warfarin therapy, undue prolongation of the prothrombin time has been the earliest manifestation of hepatitis.

Since July 1969, routine H.A.A. (Australia antigen) testing using gel-diffusion techniques has been carried out for us by Dr Y. E. Cossart of the Central Public Health Laboratory, Colindale, in all patients and staff including home dialysis patients at 3-monthly intervals and whenever there has been clinical suspicion of hepatitis in patients or staff. Since October 1970, weekly routine H.A.A. (Australia antigen) testing has been carried out in all hospital patients.

In addition, since October 1970, all patients with hepatitis at this unit have been screened for the presence of epidemic hepatitis associated antigen (E.H.A.A.), using the methods described by Del Prete *et al.* (1970).

Description of the Outbreak.—We have previously described an outbreak of hepatitis in this unit which took place from August 1966 to August 1967 (Eastwood *et al.*, 1968). This was thought to be infectious hepatitis. Following this there was a hepatitis-free interval of 14 months.

The present outbreak started in November 1968 and is still continuing at the time of writing (December 1970).

During the period from November 1968 until December 1970, 68 patients were at risk in the maintenance hæmodialysis unit, 26 were established on home dialysis after a variable period of training in the hospital unit and 12 patients on home or hospital dialysis have been transplanted. Following transplantation, a variable number of hæmodialyses in the hospital unit were necessary until adequate function of the transplanted kidney had been established. In addition, patients established on home dialysis require dialysis in the hospital unit from time to time, *e.g.* when admitted to hospital for shunt surgery.

Because of normal staff changes, over the same period of observation, 40 hæmodialysis staff including nurses, technicians and doctors were at risk in the dialysis unit. An unknown number of other personnel, *e.g.* nursing staff on other wards, surgical staff, anæsthetic staff, radiographers and physiotherapists were also at risk during this period. Twenty-eight patients developed hepatitis but only 1 member of staff, a nurse, has developed hepatitis. No deaths attributable to hepatitis occurred during the period of observation (Table I).

TABLE I

Subjects at risk from November 1968 to December 1970. An Unknown number of NonDialysis Staff were also at Risk during this Period

		Hepatitis	
	No. at Risk	Initial Attacks	Relapses
Dialysis Patients (Home, Hospital Pre-transplantation)	68	28	32
Hæmodialysis Staff	40	1	0
Total	108	29	32

Of the 28 patients who developed hepatitis, only 3 developed their initial attacks whilst on home dialysis.

Five patients had a transient slight rise in serum transaminases for 1 to 2 days immediately after renal transplantation and these have been excluded from this report.

12 of the 29 subjects who developed hepatitis had a single episode only, and in 10 of these 12 the serum transaminases were elevated for less than 1 month. In the remaining 2 subjects however abnormal serum transaminases persisted for 5 and 7½ months respectively.

The remaining 17 patients with hepatitis had between 1 to 5 biochemical relapses (rise in serum transaminases). The majority of these relapses were asymptomatic and spread over a period varying between 3 to 14 months from the onset of hepatitis.

Figure 1 summarises the outbreak of hepatitis and shows the time of onset of hepatitis in each patient together with any biochemical relapses. Maximum serum bilirubin and serum transaminase levels observed in each patient are shown in Table II.

Of the 29 patients who developed hepatitis, 14 developed symptoms at some time during their attacks. The symptoms included general malaise, fever, nausea, vomiting and/or diarrhœa.

Elevated (>0·8 mg. per cent) serum bilirubin levels were found in 8 of the 29 patients. The highest level seen was 4·5 mg. per cent in one patient (J. C.).

Role of Blood Transfusion.—The unit policy is not to give any routine blood transfusions. Transfusions are given either to replace acute blood losses or to patients who develop symptoms of anæmia. Of the 28 patients who developed hepatitis, 7 had never been transfused. Since July 1969, all blood for transfusion is screened for H.A.A. (Australia antigen) where possible. Prior screening for H.A.A. (Australia antigen) is not possible when blood transfusion is required as an emergency to replace acute blood loss.

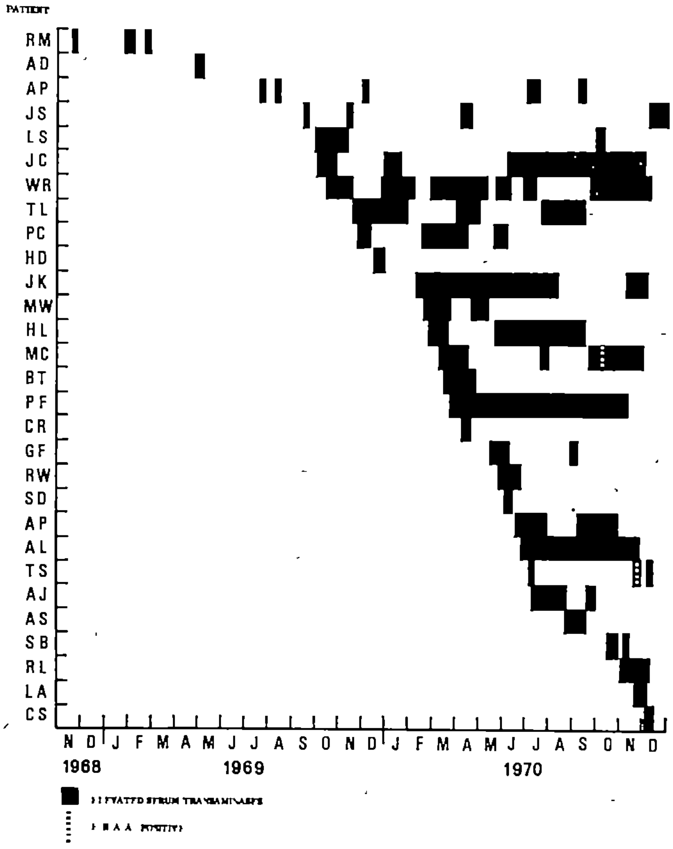

FIG. 1

This illustrates the time of onset of hepatitis in each patient together with the duration of elevated serum transaminase. Patients M. C. and T. S. were E.H.A.A. positive.

E.H.A.A. (Epidemic Hepatitis Associated Antigen) Screening and **H.A.A. (Australia Antigen) Screening in Patients with Hepatitis.**—E.H.A.A. (epidemic hepatitis associated antigen) screening became available to us during the last 3 months of the outbreak, *i.e.* October to December 1970. During this period, 16 patients developed hepatitis. Blood samples were obtained for E.H.A.A. screening from 11 of these patients during the hepatitis and were positive in two patients (M. C. and T. S., Fig. 1).

H.A.A. (Australia antigen) was not demonstrated despite repeated examination in any of the patients with hepatitis.

H.A.A. (Australia Antigen) Screening in Patients without Hepatitis.—In 1 dialysis patient, H.A.A. (Australia antigen) was detected on one occasion only, 23 months after the outbreak had started. This patient did not develop any clinical or biochemical evidence of hepatitis. Subsequent repeated examinations of his serum for H.A.A. (Australia antigen) have remained negative. No other dialysis patient or member of the staff has been shown to have H.A.A. (Australia antigen).

Other Agents as a Cause of Hepatitis.—A number of the patients with hepatitis were screened for evidence of other infections which could have been responsible for hepatitis. No evidence of glandular fever was found and all Paul Bunnell tests were negative. No evidence of active infection with toxoplasmosis or cytomegalovirus was found.

TABLE II

Maximum Serum Bilirubin and Serum Transaminases observed in Each Patient during Hepatitis

Patient	Bilirubin	S.G.O.T.	S.G.P.T.
R. M.	<0.5	77	152
A. D.	<0·5	72	>80
A. P.	<0·5	300	350
J. S.	2·5	340	340
L. S.	<0·5	290	400
J. C.	4·5	340	152
W. R.	1·7	460	680
T. L.	0·8	280	350
P. C.	<0·5	440	200
H. D.	<0·5	81	>80
J. K.	<0·5	340	510
M. W.	<0·5	300	320
H. L.	0·7	270	285
M. C.	<0·5	440	340
B. T.	<0·5	74	>80
P. F.	0·8	840	1200
C. R.	<0·5	65	130
G. F.	<0 5	63	68
R. W.	<0·5	120	290
S. D.	1 4	520	620
A. P.	<0·5	170	230
A. L.	3·8	394	>800
T. S.	<0·5	86	66
A. J.	2·2	560	410
A. S.	2·0	135	150
S. B.	<0·5	52	250
R. L.	<0·5	67	150
L. A.	<0·5	>80	>80
C. S.	1·4	280	640

Bilirubin in mg./100 ml. serum.
S.G.O.T. in Reitman Frankel units/ml. serum.
S.G.P.T. in Reitman Frankel units/ml. serum.

Effect of Hepatitis on Hæmoglobin Levels.—We have retrospectively examined the hæmoglobin levels of our patients, before and during the periods in which they had hepatitis.

Patients in whom there was a satisfactory control period before hepatitis with a stable hæmoglobin level for 2 to 5 months (mean 3·4 months) were selected.

It was possible to make satisfactory observations on hæmoglobin levels in 16 of the 28 patients who had hepatitis (Table III).

Of these 16 patients, 13 showed a rise in hæmoglobin level during the period of hepatitis and in 9 of these 13, the rise was statistically significant.

The remaining 3 patients showed a fall in hæmoglobin level during hepatitis which was statistically significant in 2.

In the 9 patients in whom there was a statistically significant rise in hæmoglobin level during hepatitis, the rise in hæmoglobin varied from 1·2–2·4 g per 100 ml. Furthermore, 7 of these 9 patients received no blood transfusions either before or during their attacks of hepatitis. In the 2 patients who required regular blood transfusions, there was a fall in the transfusion requirements during hepatitis as well as a rise in hæmoglobin level.

TABLE III

Effect of Hepatitis on Hæmoglobin Level and Transfusion Requirements in 16 Patients

	Pre-Hepatitis				During Hepatitis					
Patient	Units Blood/ month	Mean Hb	S.D.	No.	Units Blood/ month	Mean Hb	S.D.	No.	Change in Mean Hb	P (Student's *t* test)
T. L.	—	6·0	·35	8	—	8·2	1·0	16	+2·2	<0·001
J. K.	—	5·8	·69	17	—	8·2	·89	14	+2·4	<0·001
M. W.	—	7·3	7·5	7	—	8·9	1·0	3	+1·6	0·02<P<0·05
M. C.*	—	5·6	·27	14	—	7·5	·57	7	+1·9	<0·001
R. W.	—	6·9	·64	5	—	9·3	·71	5	+2·4	<0·001
A. J.	—	5·9	·89	5	—	7·9	·84	5	+2·0	0·001<P<0·01
P. F.*	—	5·5	·40	17	—	7·6	·79	18	+2·1	<0·001
P. C.*	2·5	4·5	·38	11	1·2	5·8	·92	14	+1·3	<0·001
S. B.*	1·6	4·7	1·0	20	0·6	5·9	·93	13	+1·2	0·001<P<0·01
H. L.	—	9·2	·75	6	—	10·1	1·0	12	+0·9	0·05<P<0·1 N.S.
J. C.*	—	5·6	·59	6	—	6·5	1·0	15	+0·9	0·05<P<0·1 N.S.
R. M.	0·8	5·2	·67	10	0·3	5·9	1·4	14	+0·7	0·1<P<0·2 N.S.
W. R.	0·5	6·0	·50	10	0·3	6·3	·73	24	+0·3	0·4<P<0·5 N.S.
G. F.	0·16	7·6	·46	3	0·16	6·1	·81	14	−1·5	0·001<P<0·01
J. S.	—	5·9	·71	6	—	5·0	·46	9	−0·9	0·02<P<0·05
A. L.	—	8·7	·55	3	—	7·5	1·2	11	−1·2	0·1<P<0·2 N.S.

* Anephric.

Mean Hb	Mean Hæmoglobin in G per 100 ml.
S.D.	Standard deviation.
No.	Number of observations.
P	Probability.
N.S.	Not significant.

The hæmoglobin levels after the attack of hepatitis fell gradually and reached pre-hepatitis levels 1 to 6 months after the hepatitis in 8 of the 9 patients who developed a significant rise in hæmoglobin during hepatitis. The hæmoglobin level in the remaining patient continued to rise during the 6 months following hepatitis.

Of the 16 patients studied, 5 were anephric. All 5 anephric patients had a rise in hæmoglobin level during hepatitis and in 4 of these, the rise was statistically significant.

DISCUSSION

The outbreak of hepatitis described in this unit has been relatively mild and there have been no deaths attributable to hepatitis. In addition only 1 member of staff has developed the disease.

Screening for E.H.A.A. (epidemic hepatitis associated antigen) only became possible in October 1970, that is very late in the outbreak. Already E.H.A.A. has been demonstrated in the serum of two patients with hepatitis. Del Prete *et al.* (1970) suggest that E.H.A.A. disappears rapidly from the serum of patients during convalescence. This may to some extent reduce the possibility of detection. Eastwood *et al.* (1968) describing the first outbreak of hepatitis in this unit, postulated that infectious hepatitis was responsible for that outbreak.

The finding of E.H.A.A. (epidemic hepatitis associated antigen) in the same unit during the present outbreak may be taken as further evidence that infectious hepatitis may occur endemically in some hæmodialysis units.

The relative mildness of this outbreak may be due partly to the fact that infectious hepatitis was responsible. In addition, the routine and regular administration of immunoglobulin to patients and staff in this unit may also have played a part in modifying the severity of the disease since there is now good evidence of the beneficial effect of immunoglobulin in infectious hepatitis (Pollock and Reid, 1968)

Although routine H.A.A. (Australia antigen) screening had been performed repeatedly on patients and staff during the last 18 months of the outbreak, a positive result was obtained in only one patient and on only one occasion in this patient. He did not at any time manifest any of the criteria of hepatitis. It was later ascertained that this patient, a doctor, had for a few weeks previously been working in a drug addiction centre. After H.A.A. (Australia antigen) was detected in this patient, the frequency of testing for H.A.A. was increased but with negative results in both patients and staff.

Following the report of Kolk-Vegter *et al.* (1971) on the effect of serum hepatitis on hæmoglobin levels in patients on regular hæmodialysis, we have retrospectively examined the hæmoglobin levels before and during hepatitis in some of our patients. We are able to confirm the report of Kolk-Vegter *et al.* In 9 of our patients there was a significant rise in hæmoglobin level during hepatitis. The mechanism of the rise in hæmoglobin level during hepatitis remains unknown at the present time.

SUMMARY

An outbreak of infectious hepatitis in a hæmodialysis unit is described. From November 1968 to December 1970, at least 108 patients and staff were at risk. Of the 68 patients at risk, 28 developed hepatitis. Only 1 member of the staff developed hepatitis. No deaths attributable to hepatitis occurred.

E.H.A.A. (epidemic hepatitis associated antigen) was detected in 2 patients with hepatitis. H.A.A. (Australia antigen) was not detected in any patient with hepatitis.

In one dialysis patient who had no clinical or biochemical evidence of hepatitis, H.A.A. (Australia antigen) was detected on one occasion only in October 1970.

Nine patients developed a significant rise in hæmoglobin level during hepatitis. The explanation for this is unknown.

This outbreak of hepatitis has not prevented the expansion of the home dialysis and transplantation programmes.

We are indebted to Sister P. Young and the nursing and technical staffs of the Maintenance Hæmodialysis Unit for obtaining numerous blood samples and continuing to look after the patients throughout the epidemic. Thanks are due also to Dr J. Daly and to the staff of the departments of Biochemistry, Hæmatology and Microbiology who continued to handle samples throughout the epidemic.

We are grateful to Dr Y. E. Cossart of the Central Public Health Laboratory, Colindale, for numerous H.A.A. tests. We acknowledge the assistance and co-operation of Professor S. Del Prete, Dr D. Costantino and M. Dolgia of the Istituto Clinica Medica, University of Milan.

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INCREASED SUSCEPTIBILITY OF THE KIDNEY TO ASCENDING *ESCHERICHIA COLI* INFECTION FOLLOWING UNILATERAL NEPHRECTOMY

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IN adults urinary tract infection rarely leads to progressive kidney damage in the absence of obstructive uropathy. (Freedman and Andriole, 1969; Asscher, 1970). In contrast, the late sequelæ of urinary tract infection in childhood may be more serious. Smellie and Normand (1968) showed that uncontrolled infection in children may lead to impairment of kidney growth and kidney scarring particularly when the infection is associated with vesico-ureteric reflux. These observations suggest that the growing kidneys of children may be more susceptible to the effects of ascending infection than the fully grown kidneys of adults. This hypothesis has been tested in the experimental animal by comparing the incidence of renal infection and scars following ascending *Escherichia coli* infection in animals with both kidneys *in situ* with that observed amongst animals in whom unilateral nephrectomy was performed immediately after the establishment of infection so as to produce rapid growth due to compensatory hypertrophy in the remaining kidney.

Material and Methods.—All experiments were carried out on female rats of the Wistar strain approximately 3 months old and weighing between 165 and 258 grams. The animals were fed on Oxoid diet 41B and allowed tap water ad libitum. In preliminary experiments (Asscher *et al.*, 1971) it was shown that vesico-ureteric reflux can be produced in the rat by squeezing the bladder filled with 0·25 ml. of contrast medium (" Urovision " Schering, Berlin) whilst the external urethral orifice is temporarily occluded with forceps. This procedure was, therefore, used to produce ascending urinary tract infection. A strain of *E. coli* (sero-type 0 78) which had originally been isolated from a patient with urinary tract infection was used to produce infection. The organisms were grown overnight at 37°C in Difco brain-heart infusion broth. 0·25 ml. of an N saline suspension of the organism containing approximately 10^6 bacteria was injected into the bladder which had been exposed under light ether anæsthesia through a small suprapubic incision. The bladder was then squeezed empty whilst the external urethral orifice was occluded. Sixty animals were infected in this manner. Table I summarises the experimental protocol. In half of these animals (Group 1) 1 kidney, the right or left alternatively, was excised and weighed. In the remaining 30 animals (Group 2) a sham unilateral nephrectomy was performed. The experiment was terminated 3 weeks later when total body weights and the weights of the remaining kidneys were recorded. The kidneys were removed aseptically, they were inspected, a small piece was saved for histological examination and the remainder was homogenised in a sterile all-glass tissue grinder and cultured. Urine cultures were performed weekly on all animals; the urine being obtained by suprapubic bladder aspiration.

The controls consisted of 60 animals. In 20 of these (Group 3) 0·25 ml. of N saline was injected into the bladder, the bladder was squeezed as above and a unilateral nephrectomy was performed immediately afterwards. In a further group of 20 animals (Group 4) 0·25 ml. of N saline containing 10^2 heat-killed *E. coli* 0 78 (heated to 100°C for 2 hours) were injected into the bladder and in the last of the control groups (Group 5) unilateral nephrectomy was performed and 7 weeks later, when growth due to compensatory hypertrophy had occurred to its maximum extent (Malt, 1969), ascending infection was established as above. These animals were allowed to survive for a further 3 weeks and the incidence of kidney infection and scarring was then studied as above.

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Results.—*Incidence of Kidney Scar and Infection.*—This is shown in Table I. In experimental Group 1 (ascending infection and unilateral nephrectomy) 18 of the 30 animals were found to have kidney scars. In contrast, scars were noted in only 6 of the 30 animals in Group 2 in whom sham unilateral nephrectomy had been performed. This difference was significant ($\chi^2 = 10$; $0{\cdot}01 > P > 0{\cdot}001$). The scars were invariably located in the perihilar region. A typical example is shown in Figure 1. Histologically, the scarred areas showed tubular atrophy, crowding of glomeruli and an inflammatory infiltrate consisting of a mixture of lymphocytes and polymorphonuclear leukocytes. The inflammatory infiltrate was invariably most marked in the fornices. Two of the animals in Group 5 which were infected 7 weeks after unilateral nephrectomy, were found to have kidney scars. Scars were, therefore significantly ($\chi^2 = 12{\cdot}5$; $P < 0{\cdot}001$) more common in animals which were nephrectomised immediately after intravesical administration of *E. coli* (Group 1), than in animals which were infected 7 weeks after unilateral nephrectomy (Group 5). Table I also shows the results of kidney culture in the experimental and control groups. The incidence of positive cultures closely paralleled that of kidney scars and was significantly higher in unilaterally nephrectomised than sham operated rats ($\chi^2 = 6{\cdot}4$; $0{\cdot}2 > P > 0{\cdot}01$). All scarred kidneys yielded a positive culture for *E. coli* and in a few instances positive cultures were obtained in the absence of renal scarring. Bacteriuria persisted throughout the duration of the experiment in 66 per cent of the animals of Group 1 as compared with 20 per cent of the animals in Group 2

TABLE I

Experimental Protocol and Incidence of Kidney Scarring and Infection

	Group	Number of Animals	Experimental Procedure	Number of Animals with Kidney Scars	Number of Animals with positive Kidney Culture
Experimental Animals	1	30	Ascending infection Unilateral nephrectomy	18 (60)*	20 (66)
	2	30	Ascending infection Sham nephrectomy	6 (20)	10 (33)
Controls	3	20	Intravesical administration of N. saline Unilateral nephrectomy	0 (0)	0 (0)
	4	20	Intravesical administration of heat-killed *E. coli* Unilateral nephrectomy	0 (0)	1 (5)
	5	20	Unilateral nephrectomy followed by ascending infection 7 weeks later	2 (10)	6 (30)

* Figures in parentheses refer to percentages.

and 30 per cent of the animals in Group 5. Bacteriuria persisted in all of the animals with scarred kidneys.

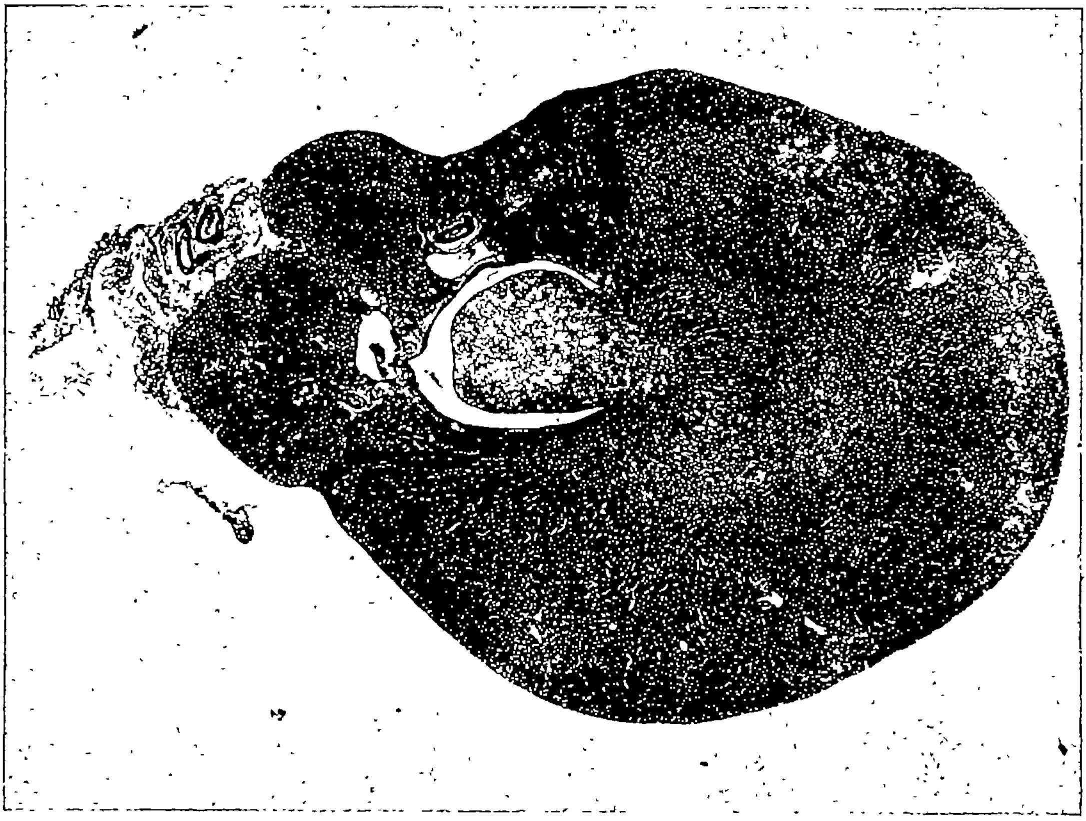

FIG. 1

Multiple scars in perihilar region of rat kidney. Transverse section ×14.5. Stained with haematoxylin and eosin.

Effect of Ascending Infection on Kidney Hypertrophy.—The changes in kidney weight following unilateral nephrectomy are shown in Figure 2. The data refer to those animals in which no evidence of renal scarring was found post-mortem. The weight change of remaining kidneys was calculated from the formula:

$$\Delta\text{KW} = \frac{\text{KW2}-\text{KW1}}{\text{BW2}-\text{BW1}} \times 100.$$

Where ΔKW = change in kidney weight expressed as a percentage of body weight.

KW_1 = weight of kidney excised initially.

BW_1 = initial body weight.

KW_2 = weight of remaining kidney 3 weeks after unilateral nephrectomy.

BW2 = final body weight.

It will be noted that even in the absence of kidney scarring, ascending *E. coli* infection produces a significant impairment of kidney growth. Thus the mean (± S.D.) weight gain of the remaining kidneys of animals in Group 3 which received N saline intravesically before unilateral nephrectomy amounted to 0·119 per cent (±0·020) as compared with a mean (± S.D.) of 0·077 per cent (±0·017) for the 12 animals in Group 1 which were infected with *E. coli* and nephrectomised but failed to develop scars. The difference between these means is significant ($t = 5{\cdot}2$; $P < 0{\cdot}001$). Even in the absence of renal scarring, therefore, ascending infection leads to impairment of compensatory growth. Administration of heat-killed *E. coli* (Group 4) also produced a significant impairment of compensatory hypertrophy as compared with that observed amongst the animals of Group 3 which received intravesical N saline before nephrectomy ($t = 5{\cdot}1$; $P < 0{\cdot}001$).

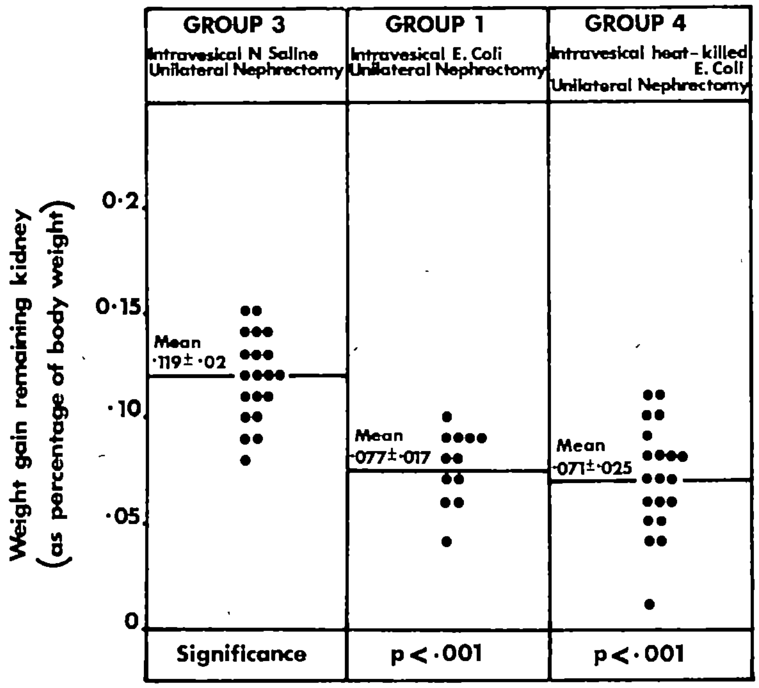

FIG. 2

Effect of intravesical administration of live and heat-killed *E. coli* on compensatory growth of rat kidney.

DISCUSSION

It has been shown that unilateral nephrectomy increases the susceptibility of the hypertrophying " opposite " kidney to bacterial invasion and scarring. Although growth due to compensatory hypertrophy is not strictly comparable with kidney growth in young animals, our observations lend support to the hypothesis that the growing kidney is more susceptible to the deletorious effects of ascending infection than the fully grown kidney.

Ascending *E. coli* infection produces 2 effects, namely scar formation and impairment of compensatory growth. Infection with live *E. coli* produces both of these effects whereas administration of heat killed organisms interferes with growth but does not lead to scarring. Kidney scars are associated with invasion of the renal parenchyma by live bacteria as evidenced by the positive cultures obtained from scarred kidneys. The cause of the impairment of kidney growth is obscure. It does not appear to result from non-specific growth retardation due to a reduction of food intake by the infected animals since measurement of food intake and body weights of the infected and control groups revealed no significant differences. It may be that the impairment of kidney growth is due to an effect of *E. coli* endotoxin. This suggestion receives support from the observation (Asscher and Chick, in preparation) that the impairment of compensatory hypertrophy produced by heat-killed *E. coli* 0 78 can be prevented by previous immunisation using a heat-killed *E. coli* 0 78 vaccine. It may be concluded that the 2 effects of ascending infection on the hypertrophying kidney (impairment of growth and scarring) do not share a common pathogenesis and that they may, therefore, require different means of prevention and treatment. This conclusion may also be relevant to the prevention and treatment of the late sequelæ of ascending urinary tract infection in childhood.

SUMMARY

Renal infection and scarring following ascending *Escherichia coli* infection occurs more frequently in unilaterally nephrectomised rats than in sham nephrectomised animals. When ascending infection is established 7 weeks after unilateral nephrectomy at a time when compensatory growth of the remaining kidney is complete, no increase in the incidence of renal infection and scarring is noted. These observations show that growth due to compensatory hypertrophy sensitises the kidney to bacterial invasion and scarring. Ascending infection produces 2 separate effects on the hypertrophying kidney, namely impairment of growth and scar formation. Scar formation is associated with bacterial invasion of the renal parenchyma whereas impairment of growth may be due to an effect of bacterial endotoxin.

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TRANSURETHRAL TREATMENT OF URETEROCELES

A Report on 45 Cases mostly treated by Transurethral Resection

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TRANSURETHRAL treatment of ureteroceles is a simple and effective method of treatment (Thompson and Green, 1942; Raper, 1958; Aas, 1960). The methods usually used are partial or complete resection of the ureterocele down to bladder muscle, or incision, which may be combined with diathermy of the incised edges. Little advantage is gained by open excision alone, and it shares with endoscopic forms of treatment, especially in children, the disadvantage that vesico-ureteric reflux may occur post-operatively (Thomspon and Kelalis, 1964; Roylance and Roberts, 1965; Roper and Smith, 1965; McAdam and James, 1967).

Asymptomatic ureteroceles occur, but usually a ureterocele causes upper urinary tract back-pressure which may be complicated by urinary infection or stones, either in the ureterocele or in the ipsilateral ureter or kidney. These complications may demand further operations on the kidney or ureter.

Rarely chronic retention due to obstruction of the vesical outlet by a large ureterocele and contralateral ureteric obstruction occur. Prolapse of the ureterocele into the urethra can cause acute retention (Gaganakis, 1960) and in females may present as a vulval swelling (Kickham, 1944).

Reports of series of ureteroceles are uncommon. Series published in the last decade include those of Wallgren and Salmi (1961) 21 cases, Thompson and Kelalis (1964) 176 cases, Roylance and Roberts (1965) 27 cases, and Hutch and Chisholm (1966) 4 cases. Uson (1961) proposed a classification of ureteroceles in children, and recently Johnston and Johnson (1969) have described their experiences of 31 children with ectopic ureteroceles.

Endoscopic incision of ureteroceles has been frequently reported (Thompson and Green, 1942; Aas, 1960; Raper, 1960; Swinney, 1963; Thompson and Kelalis, 1964). Zielinski (1962), concerned by the development of vesico-ureteric reflux in 5 of 10 treated cases (4 endoscopic incision, 1 open excision), suggested a transverse endoscopic incision to leave the length of the roof of the intravesical ureter unchanged while the orifice was broadened.

Transurethral resection, while mentioned in some papers, is advocated less often and comparisons with transurethral incision are not made. Begg (1948) advised endoscopic excision of the largest possible slice with a cutting loop, while Aas (1960) reported the resection of 12 of 35 cases treated transurethrally. Thompson and Kelalis (1964) used the Thompson resectoscope alone or in combination with a Colling's knife in 25 of 104 ureteroceles in adults. Swinney (1963) has partially resected a large part from the ureterocele wall in adult cases to prevent stenosis of the ureteric orifice.

The transvesical approach is sometimes indicated for large ureteroceles (Kickham, 1944) and in the rare case where associated stones are too big for litholapaxy (Thompson and Green, 1942). It may also be resorted to where cystoscopic diagnosis or assessment has not been possible, where complete nephro-ureterectomy is planned, if instrumentation is difficult, or the facilities for endoscopic surgery are not available. Hutch and Chisholm (1966) favour the incorporation of anti-reflux principles into operations, allowing the removal of obstruction without causing reflux. They advise inferior meatotomy performed through a cystostomy for small ureteroceles, and a uretero-vesicoplasty similar to the Bishoff operation for the larger ones. They concluded that all the standard anti-reflux operations would combine satisfactorily with excision of the ureterocele and cited Paquin's report of a successful case complicated by double ureters.

In children, nephro-ureterectomy is often required because of gross renal damage at the time of presentation (Williams, 1958; Raper, 1960), especially those with ectopic ureteroceles. Where useful function remains, the child can have transvesical uncapping of the ureterocele combined with a reflux preventing uretero-neo-cystostomy. Johnston and Johnson (1969) believe endoscopic incision to be inadvisable in children with ectopic ureteroceles, but resection, by removing any obstructing tissue, may be worth a trial before nephro-ureterectomy.

This series may be of interest as the majority were treated by transurethral resection using a Stern MacCarthy resectoscope.

Material.—Forty-five patients were admitted for surgical treatment of ureteroceles to the Urological Department, Meath Hospital, Dublin, in the period 1952 to June 1970 inclusive.

TABLE I

Age Distribution (45 cases)

0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80+
5	2	13	13	6	2	3	1	0

TABLE II

Presenting Symptoms (45 cases)

	Total	Alone
Loin pain	30	15
Dysuria	20	1
Hæmaturia	17	3
Frequency	15	3
Incontinence	2	...
Recurrent epididymitis	1	...

Those patients diagnosed radiologically or cystoscopically who, because of lack of symptoms or complications, did not warrant treatment are not included. Eight patients had bilateral ureteroceles, 5 in females, 3 in males, making a total of 53 ureteroceles. Thirty-two occurred in females and 21 in males. Thirty were situated on the right and 23 on the left. The age distribution of the patients at the time of presentation is shown in Table I, and their presenting symptoms in Table II.

Radiological Investigation.—The typical halo or " cobra head " was seen in the cystograms of the intravenous pyelograms in 25 ureteroceles (Fig. 1). The diagnosis was suspected in 8 and in 20 the excretory cystogram was normal.

Of the 51 sides visualised by intravenous urography, 34 showed varying degrees of upper tract dilatation on the side of the ureterocele. In 18 this was confined to the lower third of the ureter, but in 24 hydronephrosis was present on that side. Two kidneys showed no radiological function. Pyelonephritic changes in the kidney on the affected side were present above 10 ureteroceles.

Congenital anomalies of the upper urinary tract were often observed on the side of the ureterocele: these were duplex kidneys and ureters 8, duplex pelvis 1, hypoplasia 2, and pelvi-ureteric junction obstruction 1. The contralateral side showed duplex kidneys and ureters 1, agenesis 1, and pelvi-ureteric junction obstruction 1.

Calculi were observed in 9 ureteroceles. Two cases had vesical stones, while ureteric stones were present in 2 cases above the ureteroceles. Renal stones were present in 7 kidneys above a ureterocele. In 2 cases the renal stones were bilateral although the ureteroceles were unilateral. One of the ureteroceles was discovered during the investigation for nephrocalcinosis due to a parathyroid adenoma. Stone formation progressed on both sides despite return to normal serum calcium level following parathyroidectomy and resection of the unilateral ureterocele. Investigation of the calcium metabolism in the other cases was normal. Micturating cystography was performed in one case pre-operatively and no reflux was seen.

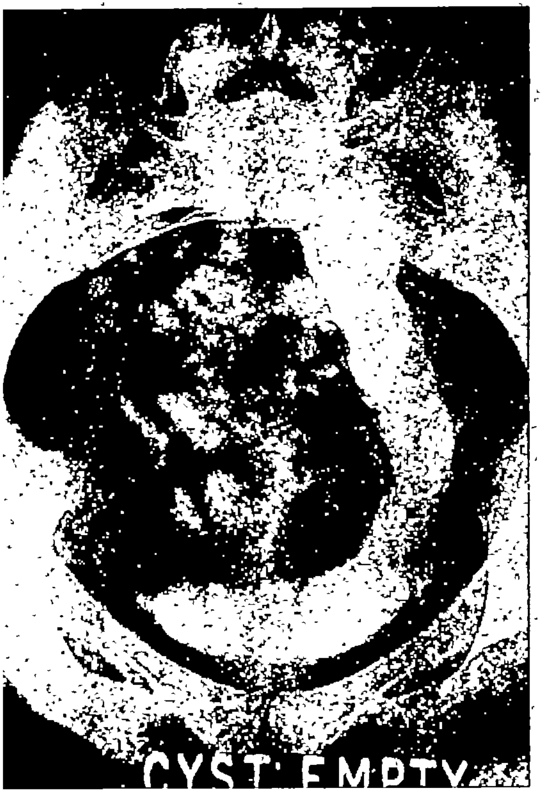

FIG. 1

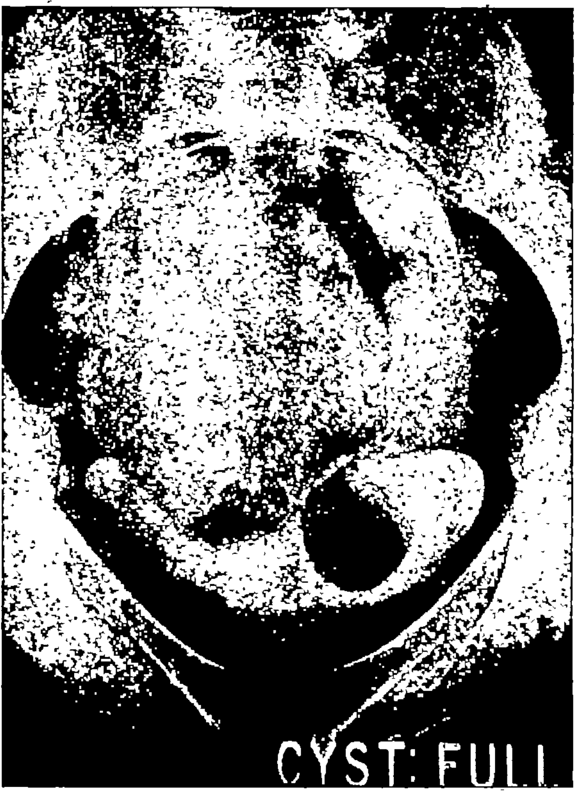

FIG. 2

Fig. 1.—Left-sided ureterocele with ureteric dilatation. No reflux followed transurethral resection in this case.

Fig. 2.—Bilateral ureteroceles with duplex ureters.

Endoscopic Findings.—All cases were confirmed cystoscopically. No ectopic ureteroceles were found. Ureteroceles were described as being small in 13 cases, moderate in 2, large in 6 and massive in 1. In the remainder no comment was made on the size. In 2 cases the cystoscopic appearance suggested associated neoplasm, but biopsy revealed acute inflammation in a stone-bearing ureterocele in one and tuberculosis in the other.

Infection.—Urinary infection was present in 18 cases at the time of presentation, 16 being Gram-negative and 2 Gram-positive organisms. The urine was sterile in 23 cases and the results of culture not recorded in 4.

Treatment.—Primary treatment was directed at the ureterocele by endoscopic means in all cases. The methods employed were:

Transurethral resection of ureterocele (resection)	39
Transurethral incision of ureterocele (incision)	11
Litholapaxy of stone from ureterocele	3
No treatment (bilateral cases, one side only treated)	2

In 1 case, where the intravenous pyelogram had confirmed a large stone in the ureterocele, cystoscopy following an episode of severe ureteric colic, frequency and dysuria, showed a large, ragged ureteric orifice on the side where the ureterocele had been visualised and the stone within the bladder. Litholapaxy was required for its removal. Presumably the stone had ulcerated through the wall of the ureterocele, thus curing it.

Technique.—Transurethral resection of the ureterocele was performed using the Stern MacCarthy resectoscope. The ureteroceles were resected flush with the bladder wall, the largest producing 23 g. of tissue. The presence of stones made cutting more difficult, but once unroofed, these could be levered into the bladder and the resection completed. Recovery of stones was usually through the resectoscope, but some were removed through the Braasch cystoscope, using the Bumpus specimen taker. Three stones required litholapaxy for their removal. Transurethral incision was made in the line of the ureter with a Colling's knife, a cutting electrode through the panendoscope, or with a resectoscope knife. The incision included the ureteric orifice if this was visible and conveniently situated.

Post-operative catheter drainage was continued usually for 48 hours and the procedure performed under antibiotic cover in the infected cases. In the bilateral cases a period of 3 weeks was usually allowed before proceeding with the second side.

Post-operative bleeding warranting return to theatre, evacuation of clots and diathermy to bleeding vessels occurred in 3 cases, following resection (2 days), resection+litholapaxy (6 days), and an incision (8 days).

Pathology.—Histological examination of 32 specimens following resection was performed. These showed evidence of inflammation in 20 (1 acute, 19 chronic), œdema 11, squamous metaplasia 3, nests of von Brunn 2, tuberculosis 1, columnar combined with transitional epithelium 1. Twelve specimens contained muscle and it is of interest that the case where the thickness of the muscle was commented upon was one of the four ureteroceles shown to develop vesico-ureteric reflux after treatment, and one of the two which developed a renal stone following operation.

Follow-up.—Forty-three of the 45 patients were followed up for a period of 3 months to 17 years, with an average of 3 years 4 months. Two patients were not seen following discharge from hospital.

Symptoms.—Of the 31 patients with 37 ureteroceles seen following treatment by resection, 21 required this treatment alone for symptomatic cure. Secondary operations for the relief of loin pain were performed in 3 cases (pyelolithotomy 1 case, transurethral manipulation of ureteric stone 1 case, division of aberrant vessels 1 case). Two further cases required nephrectomy to relieve the symptoms of recurrent urinary infection. Both patients requiring nephrectomy following primary treatment (both resection) had had ureteric meatotomies, and 1 a ureteric dilatation as well. These produced only transient improvement in the upper tract dilatation, but no change in the recurrent urinary infection for which nephrectomy was necessary.

Seven of the 11 patients were symptomatically cured by incision alone. One was later relieved of loin pain following pyelolithotomy, and another of the symptoms of urinary tract infection by nephrectomy. One patient, although symptomless following incision, had a nephrectomy because of absence of radiological renal function.

Six patients had persistent symptoms, 4 following resection, 1 after incision and 1 after resection and later nephrostomy. In all cases but one loin pain was the complaint, but frequency due to recurrent urinary tract infection has persisted in one patient (resection).

As observed by Raper (1958), symptoms sometimes took time to subside. Most of the uncomplicated cases were asymptomatic at the first follow-up appointment 3 months after treatment, but 2 cases were not relieved of loin pain for 3 years. Raper (1960) recommended a period of observation between primary operation on the ureterocele and eventual operation on the kidney.

Infection.—Eradication of infection following endoscopic treatment of the ureterocele as demonstrated by absence of infection after a maximum of 2 courses of antibiotics was seen in 12 of the 18 cases infected pre-operatively. No case of persistent infection developed where the urine was sterile pre-operatively. The persistent infections followed resection (5 cases) and incision (1 case). but 1 was associated with tuberculosis and 1 with renal stone. It is of interest to note that in all 4 cases treated by nephrectomy early in the series part of the ureteric stump was left *in situ*. Two cases, later submitted to nephrectomy, on whom micturating cystography had been performed following endoscopic treatment of the ureterocele, showed no reflux, but all have been cured of infection and symptoms. Total nephro-ureterectomy is now advised (Amar, 1964; Johnston and Johnson, 1969) to avoid the possibility of stump infection.

Radiological Follow-up.—Radiological follow-up was performed on 41 patients following initial transurethral treatment of 47 ureteroceles. No recurrences were seen. The radiological appearance of the two untreated sides remain unchanged.

Upper tract dilatation improved in 29 cases (resection 23, incision 6), remained unchanged in 10 (resection 7, incision 2, 1 "self cure"), and increased in 6 (resection 5, incision 1). Two kidneys remained radiologically non-functioning. Following treatment the intravenous pyelogram assessment of the upper tract dilatation was normal 23 (pre-operative 8), lower third ureterectasis 10 (pre-operative 18), ureterectasis 0 (pre-operative 1), hydronephrosis 14 (pre-operative 24), and no function 2 (pre-operative 2).

Five kidneys were seen to develop radiological changes compatible with chronic pyelonephritis, the earliest 8 months, the latest 6 years after primary treatment. Four followed resection, of which 3 were associated with pre-operative calculi, and one had developed a renal stone 26 months following operation. Only 1 (resection) had shown persistent infection, and 3 of the 5 had demonstrated improvement in previous upper tract dilatation.

Two patients developed renal calculi following transurethral resection of the ureterocele on that side. Both occurred in the lower calyx, 1 following the division of aberrant vessels for hydronephrosis (previous resection of ureterocele), the other after resection where reflux was shown post-operatively.

Three patients passed stones spontaneously from the upper tract after endoscopic treatment, in one a string of 5 stones in a ureter all passed. No recurrence of stone has occurred following the 2 pyelolithotomies but 7 patients remain with asymptomatic renal stones (5 pre-operative, 2 post-operative).

Micturating cystography was performed post-operatively on 10 occasions in 8 patients. It was done 7 times following resection alone, once following resection and again later after meatotomy and ureteric dilatation. The results are shown in Table III. Another patient, not included in this series, but having had a ureterocele treated by incision elsewhere, showed no vesico-ureteric reflux during a micturating cystogram performed because of loin pain.

Two cases (1 resection, 1 resection and later meatotomy and ureteric dilatation) showed increased upper tract dilatation in the absence of reflux. Both were children with gross upper tract dilatation and recurrent urinary infection where endoscopic treatment was tried prior to nephrectomy. Three (3 resection—1 bilateral) showed no change or improvement despite the development of post-operative reflux. A repeat examination 4 months later in the bilateral case

TABLE III

Retrograde Micturating Cystography following Primary Endoscopic Treatment of Ureteroceles

Name	Age	Operation	Duration following Primary Treatment	Reflux	Indication	Pre-op. Upper Tract	Post-op. Upper Tract	Comment
P. O'S.	34	Resection.	10/12	None.	Loin pain.	Lower 1/3 ureterectasis.	Unchanged.	Asymptomatic. No infection.
N. L.	21	Resection.	Same day.	None.	Non-functioning kidney.	Not demonstrated.	Not demonstrated.	Hypoplastic kidney. (Aortogram.)
S. C.	1½	Resection.	2/12	None.	Recurrent infection.	Hydronephrosis.	More dilated.	Nephrectomy.
C. C.	33	Resection.	11/12	None.	Loin pain.	Hydronephrosis.	Less dilated.	Asymptomatic. No infection.
J. R.	5	Resection.	8/12	None.	Recurrent infection.	Hydronephrosis.	More dilated.	
		Meatotomy.	4/12	None.	Recurrent infection.	Hydronephrosis.	More dilated.	Nephrectomy.
G R.	23	Resection.	3 years.	Reflux to sacral segment.	Developed renal stone.	Hydronephrosis.	Unchanged.	Asymptomatic. No infection. Thick muscle in resected specimen.
J. L.	39	Resection (bilateral).	R. 2/12 L. 4 days	Reflux to both upper segments of duplex kidneys.	Loin pain.	Hydronephrosis.	Less dilated.	Now asymptomatic. No infection.
			R. 6/12 L. 4/12	Right upper segment only.	Loin pain.	Hydronephrosis.	Less dilated.	
G. G.	4	Resection.	10/12	Gross reflux to kidney.	Failure of hydronephrosis to decrease.	Hydronephrosis with marked cortical loss.	Unchanged.	Asymptomatic. No infection.
D. R.	24	Incision (elsewhere).	14/12	None.	Loin pain.	...	Normal.	Now asymptomatic. No infection. Normal I.V.P.

TABLE IV

Operations on Upper Tract after Primary Endoscopic Treatment of Ureterocele

Patient	Age	Previous Operation	Operation	Duration following Primary Operation on Ureterocele	Indication	Result	Comment
M. O'D.	16	Incision.	Pyelolithotomy.	10 days.	Loin pain.	Asymptomatic. No infection.	No recurrence of stone.
E. N.	4	Incision.	Nephrectomy.	5/52	No function.	Asymptomatic. No infection.	Hypoplastic kidney. No glomeruli. Not total ureterectomy.
M. O'R.	42	Resection.	T.U. removal of ureteric stone.	5/12	No progression of stone. Partial ureteric obstruction.	Asymptomatic. No infection.	Developed chronic pyelonephritis.
C. C.	50	Resection.	Pyelolithotomy.	2/53	Pain right loin. Hæmaturia.	Asymptomatic. No infection.	No recurrence of stone. Chronic pyelonephritis.
C. C.	25	Resection.	Division of aberrant vessels.	12/12	Loin pain.	Asymptomatic. No infection.	Stone appeared in kidney 26/12 later.
J. G.	1½	Incision.	Nephrectomy.	1/12	Recurrent infection.	Asymptomatic. No infection. at 3/12 post-op.	Histology—" dysgenesis " with foci of chronic pyelonephritis. Not total ureterectomy.
S. C.	1½	Resection. Meatotomy.	Nephrectomy.	4/12	Recurrent infection.	Asymptomatic. No infection.	Not total ureterectomy. (No reflux.)
J. R.	5	Resection. Meatotomy Dilatation of ureter.	Nephrectomy.	15/12	Recurrent infection.	Asymptomatic. No infection.	Not total ureterectomy. (No reflux.)
E. W.	66	Resection.	Nephrostomy.	2/12	Increased dilatation. Failure to catheterise ureteric orifice.	Loin pain. Persistent infection.	Tuberculosis. Survived with nephrostomy for 7 years. Contra-lateral nephrectomy for tuberculosis.

showed the reflux into the upper segment of one duplex kidney where previously this had been bilateral. No case in which the micturating cystogram showed vesico-ureteric reflux has developed radiological changes of pyelonephritis, but 1 case with reflux developed a renal stone.

Post-operative Cystoscopy.—Cystoscopy was performed following initial treatment in 17 cases. No recurrence was seen. The earliest was 2 days (resection) and 8 days (resection) post-operatively, when the orifices were described as " œdematous " and " inflamed ". Another (resection), seen prior to resection of the contra-lateral side 3 weeks later, was described as a " linear necrotic area ". In the remainder the mucosal covered orifices were described as " normal " 2 (resection), " wider than normal " 6 (3 resection, 3 incision), " small with difficulty in introducing catheter " 2 (both resection), " mucosal bridge across orifice " 1 (resection), " two ureteric orifices " 1 (resection), " not seen " 1, and " no comment " 1. Operations considered necessary on the upper tracts following primary treatment of the ureteroceles in our series are shown in Table IV.

DISCUSSION

Transurethral resection of a ureterocele can usually be relied upon to relieve ureteric obstruction and to decrease the admittedly small likelihood of recurrence, but Aas (1960) described 2 recurrences in 43 surgically treated cases (transvesical incision 1, transvesical incision and partial resection 1). Resection also gives good results where large, adult ureteroceles are causing vesical neck obstruction.

The theoretical disadvantages of resection are that it may be unnecessary, be more hazardous, may interfere with the uretero-vesical junction of an associated " normal " ureter in duplex cases, and replace obstruction of the ureteric orifice with vesico-ureteric reflux by shortening the roof of the intravesical ureter (Paquin, 1959), by removal of the shearing action of the longitudinal muscle of the intravesical ureter (Stephens and Lenehan, 1962), by interfering with the normal function of the trigonal muscles (Tanagho and Pugh, 1963), by distorting the posterior supporting layers (Castro and Fine, 1969), and interfering with their pinchcock action (Urlenhoth, Hunter and Loechel, 1952).

Rees (1969) demonstrated a high incidence of reflux following resection of bladder tumours in the region of the ureteric orifices, and emphasised the need for early detection and treatment of bladder neck obstruction. Complete removal of neoplasm often involves removal of the intravesical ureter and resection or diathermy of the surrounding vesical muscle. However, during resection of a ureterocele the dilated intravesical ureter can be removed, leaving the deeper structures intact.

The incidence of reflux following resection in this series suggests that the intravesical ureter, at least in some cases, does not play a dominant role in the preservation of vesico-ureteric continence and that resection of the ureterocele does not interfere with other postulated mechanisms. This is not supported by the figures of Roylance and Roberts (1965) who demonstrated reflux in 7 of 15 ureters treated in their own series, and 24 of 55 from a collected series, but do not mention the type of endoscopic treatment used. The explanation may be that, especially in small cases, enough intact intravesical ureter remains above the resected ureteroceles to help maintain continence. Three of the 4 cases in our series, where resection was followed by reflux, were large ureteroceles, presumably involving the whole length of the intravesical ureter.

Pre-operative micturating cystography is not commonly performed in this condition so the true incidence of reflux is not known. Aas (1960) described a case where reflux occurred pre-operatively but had had previous diathermy to areas of tuberculous cystitis. Wallgren and Salmi (1961) and Roylance and Roberts (1965) reported 3 and 2 cases respectively which, like our case, showed no reflux. Johnston and Johnson (1969) discussed the significance of reflux into associated twin and contra-lateral ureters, but do not mention reflux into ureters above their ectopic ureteroceles, although Williams (1958) says it may occur into a dilated ureter following micturition.

Micturating cystourethrography has been advocated post-operatively in all cases (Roylance and Roberts, 1965; Roper and Smith, 1965) but in the absence of symptoms, infection, or other complications it seems hardly justified in the majority of cases and the known variability of reflux (Emmett, 1964; Hodson, 1969) and its tendency to decrease with time (Thompson and Kelalis, 1964) would decrease the significance of the routine use of the procedure.

If reflux occurs following endoscopic treatment and is shown to be harmful, open surgical revision of the uretero-vesical junction can be performed, but even then cure cannot be guaranteed, especially in the presence of ureteric dilatation, infection at the time of operation, and bladder neck obstruction (Nanninga *et al.*, 1969).

The prognosis of the kidney above the ureterocele is largely determined by the presence of complications at the time of presentation. The 4 cases requiring nephrectomy were all children, 3 having marked upper tract dilatation, loss of renal cortex and recurrent infection before primary treatment; the other had a hypoplastic kidney which histologically showed absence of glomeruli.

The 5 cases showing increased dilatation following treatment (4 resection, 1 incision) all had ureteric dilatation pre-operatively, 1 had a transurethral removal of a ureteric stone performed, 1 was associated with bilateral renal stones, 1 had tuberculosis, and 2—in retrospect—should possibly have been treated primarily by nephro-ureterectomy.

Of the 5 cases shown to develop radiological changes of pyelonephritis, 3 had renal stones present pre-operatively, 1 later developed a renal stone (resection), and 1 (incision) remains free of stone. Four of these 5 cases have remained free of infection following endoscopic treatment of the ureterocele.

In only 2 cases previously free of complications, apart from upper tract dilatation, does treatment of the ureterocele appear to have been detrimental in the long term. One developed reflux, then a stone, following resection; the other developed radiological changes of pyelonephritis following incision.

The bilateral cases all responded well to treatment. Pre-operatively none developed stone, and pyelonephritic changes developed in only 3 kidneys. All were symptomatically relieved by primary treatment (13 resection, 1 incision, 2 no treatment), no operations being required on the upper tracts. All post-operatively remain free from infection and none have been seen to develop calculi or radiological pyelonephritis.

SUMMARY

1. The endoscopic treatment of 51 ureteroceles is described. 39 were treated by transurethral resection, 11 by transurethral incision and 1 underwent a " spontaneous cure ".

2. A comparison is made between the results of incision and resection showing that while incision is simple and effective, transurethral resection is also a reliable method of treatment, especially in the uncomplicated adult cases, so long as the resection is confined to the ureterocele and the underlying vesical muscle left intact.

3. The prognosis in bilateral adult ureteroceles is good.

We wish to thank Mr V Lane, who dealt with many of these cases, for his co-operation.

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CHEMOTHERAPY FOR METASTATIC TERATOMAS OF THE TESTIS

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IN 1955 Wildermuth reported regression of lung metastases from a tumour of the testis treated with nitrofurazone, but the histology was not given. The present advance of successful chemotherapy for disseminated tumours of the testis followed the work of Li, Whitmore, Golbey and Grabstald (1960) at the Memorial Hospital, New York, who used actinomycin D, chlorambucil and methotrexate; in their first series of 36 patients, 15 responded and 6 showed complete regression of lung metastases. Mackenzie (1966) at the same hospital later reviewed their work and from a larger series concluded that actinomycin D had been the most effective drug; he was the first to report tumour regression with this alone. In 1960 Curreri and Ansfield had reported the first success with mithramycin alone in a patient with a metastatic tumour presumed to be from the testis. Kofman *et al.* (1964), Ream *et al.* (1968), and several others also had success with mithramycin alone, reporting good regressions but severe toxicity; a mortality rate as high as 25 per cent (3 out of 12 patients) had been reported by Brown and Kennedy in 1965. Kennedy (1970) modified the mithramycin treatment using an alternate-day plan, and succeeded in eliminating the drug-induced mortality and reducing the toxicity. It thus became clear that patients with disseminated teratomas of the testis might respond to the anti-tumour antibiotics in somewhat the same way as do children with embryonal sarcomas.

Other drugs, mostly used in combinations, were tried by many. Assessment of effectiveness is difficult here because of the many partial and temporary regressions reported. Brief regressions can in fact be induced in a variety of tumours by large doses of cytotoxic agents; if all such hesitations in tumour growth and partial responses are to be considered, then the pattern of favourable response to effective drugs is likely to be obscured. Reports of complete, chemotherapy-induced remissions—that is, disappearance of all clinical and radiological evidence of metastatic disease—are now sufficiently numerous to be the subject of a more profitable assessment. Some of these remissions have lasted long enough for the patients to be regarded as cured, especially as a 2-year, completely disease-free period with these particular tumours is an indication that further recurrence is improbable. Shorter remissions, if complete, may provide opportunities for studying weaknesses in technique which might perhaps have been more successful if a better combination of drugs, improved timing of courses, or longer duration of treatment following a full remission had been adopted.

Chemotherapy for seminomas of the testis should not be necessary since adequate treatment from the first by orchidectomy and radiotherapy is curative (Smithers *et al.*, 1971). Only in a few patients, where there has been neglect or mismanagement, does spread beyond control of irradiation occur. For these tumours, chlorambucil has been the drug most generally employed. However, as chemotherapy is rarely needed for seminomas, evidence of its value is difficult to obtain, but complete remissions have been reported (Mackenzie, 1966). A trial of melphalan (sarcolysin) in Russia (Blokhin *et al.*, 1958) showed good responses in patients with seminomas. In 1961, I was able to see a number of patients being treated in their clinic with melphalan with some success. However, a cure-rate of over 90 per cent can be obtained with routine post-operative irradiation. The particular value of this Russian work was to demonstrate that seminomas could respond well to chemotherapy. Seminomas have responded to cyclophosphamide as well as to chlorambucil and melphalan.

This paper summarises the published evidence for complete remission of all detectable metastatic disease after chemotherapy in teratomas of the testis by tumour type and by chemotherapeutic agents employed, in an attempt to discern the most effective drugs and drug combinations that have been used.

Classification.—The classification of tumours of the testis agreed by the Testicular Tumour Panel of Great Britain differs in some respect from that of the Armed Forces Institute of Pathology in Washington which has been widely adopted in the United States. The 2 sections dealing with teratomas of the testis are each set out here for comparison.

Armed Forces Institute of Pathology		Testicular Tumour Panel of Great Britain
Teratoma	↔	Teratoma Differentiated
Teratocarcinoma	↔	Malignant Teratoma Intermediate
Embryonal Carcinoma	↔	Malignant Teratoma Anaplastic
Choriocarcinoma	↔	Malignant Teratoma Trophoblastic
Teratoma with Seminoma	↔	Combined Tumour

The intermediate teratomas of the British classification are divided into A and B grades. Most of the teratomas of the more malignant B grade are classed as embryonal carcinomas rather than as teratocarcinomas in the United States classification. The few combined tumours included in this review have been classified according to their teratomatous elements. As so much of the published work on the chemotherapy of testicular tumours comes from the United States, the terminology of the Armed Forces Institute of Pathology has been retained in the tables.

Survey of Published Work.—Table I sets out the accepted complete remissions after chemotherapy of metastatic disease in patients with teratomas of the testis gleaned from the literature.

TABLE I

Metastatic Teratomas of the Testis: Complete Remission after Chemotherapy
Data from 18 Reports[1] published 1960-1970

Histology of Primary Tumour	No. of Patients	Range of Duration of Remission in Months
Embryonal carcinoma	50	114— 3
Uncertain, probably embryonal carcinoma	9	49— 2
Choriocarcinoma	5	92—35
Teratocarcinoma	1	10
	65	Remission lasted more than 2 years in 25 patients; more than 5 years in 11 patients

[1] See References.

Complete remission has been taken as disappearance of all clinically and radiologically detectable signs of disease in patients having good evidence of metastatic disease as reported, who have been observed in complete remission for a minimum period of 2 months. Patients having radiotherapy at the same time as chemotherapy or in whom there was only a raised gonadotrophin excretion to suggest metastasis, or cases where the histology, duration of remission or drug combinations used were not clearly given, have been omitted.

TABLE II

Metastatic Embryonal Carcinomas of the Testis: Complete Remission after Chemotherapy. Data from 17 Reports[1] published 1960-1970

Duration of Complete Remission	No. of Patients
More than 8 years	2
5 to 8 years	6
2 to 5 years	10 (2)
1 to 2 years	17 (2)
Less than 1 year	10 (5)
Only mean duration known	5
	50 (9)

[1] See References.

Nos. of patients with tumours of uncertain histology presumed to be embryonal carcinomas are given in brackets.

TABLE III

Metastatic Embryonal Carcinomas of the Testis: Complete Remission after Chemotherapy. Data from 11 Reports[1] published 1960-1970

A Drugs, used alone	No. of Patients with Complete Remissions	Range of Duration of Remission in Months
Mithramycin	17	84— 2
Actinomycin D	5	21— 9
Vinblastine	4	45— 5
Methotrexate	2	96—72
Nitrofurazone	2	12— 4
Hydroxyurea	1	4
	31	Remission lasted more than 2 years in 9 patients

[1] See References

Complete remissions have followed the administration of certain drugs given alone—A drugs—namely actinomycin D, mithramycin, methotrexate, vinblastine, nitrofurazone and hydroxyurea, and of drugs which have been concerned with complete remissions only when given in various combinations—B drugs. All successful mixtures containing B drugs have contained at least one of the A drugs. The B drugs are vincristine, chlorambucil, cyclophosphamide, melphalan, nitrogen mustard and 5-fluorouracil.

TABLE IV

Metastatic Teratomas of the Testis: Complete Remission after Chemotherapy
Data from 9 Reports[1] published 1963-1970
A drugs are shown in italics

11 Drugs used in 10 Different Combinations	No. of Patients with Complete Remissions
Actinomycin D, Methotrexate and Chlorambucil	13
Actinomycin D and Chlorambucil	5
Methotrexate, Vincristine, Cyclophosphamide and 5-fluorouracil	5
Actinomycin D, Mithramycin, Vincristine and Cyclophosphamide	3
Methotrexate and Nitrogen Mustard	2
Vinblastine and Melphalan	2
Actinomycin D and Nitrogen Mustard	1
Actinomycin D, Vincristine and Cyclophosphamide	1
Methotrexate, Vincristine and Melphalan	1
Methotrexate, Nitrofurazone and Chlorambucil	1
	34

[1] See References.

TABLE V

Metastatic Teratomas of the Testis: Complete Remission after Chemotherapy
Data from 18 Reports[1] published 1960-1970

Drugs used	Complete Remissions		
	When used Alone for 31 Patients	When used in 10 Combinations for 34 Patients	No. of Times used Successfully for 65 Patients
A Drugs			
Actinomycin D	5	23	28
Methotrexate	2	22	24
Mithramycin	17	3	20
Vinblastine	4	2	6
Nitrofurazone	2	1	3
Hydroxyurea	1	0	1
B Drugs			
Chlorambucil	0	19	19
Vincristine	0	10	10
Cyclophosphamide	0	9	9
5-fluorouracil	0	5	5
Melphalan	0	3	3
Nitrogen Mustard	0	3	3

[1] See References.

TABLE VI

Metastatic Teratomas of the Testis. Intermediate B and Anaplastic (Embryonal Carcinomas) Treated by Chemotherapy at the Royal Marsden Hospital, 1962-1967

Of 18 patients, 12 have died: 2 Stage I patients died at 24 and 14 months,
3 Stage II patients died at 25, 7 and 6 months,
2 Stage III patients died at 12 and 3 months,
5 Stage IV patients died at 8, 7, 6, 3 and 3 months.
6, details below, had remissions, 3 attributed to chemotherapy alone, 3 to maturation and surgery.

Case No.	Age	Stage when First Treated	Time in Months to Detection of Spread	Treatment for Metastases	Duration of Remission in Months	Time of Observation from First Treatment
1	27	IV	0	Actinomycin D	84	7 years. Alive
2	28	III	1	Actinomycin D Provera	61	5½ years. Alive
3	33	II	9	Actinomycin D	2½ and 3	2½ years. Dead
4	44	II	39	Actinomycin D Provera Cyclophosphamide Surgery	35	7 years. Alive
5	45	I	10	Actinomycin D Provera Surgery	36	4½ years. Alive
6	19	I	56	Surgery Actinomycin D Provera Testosterone Vincristine Natulan Nitrogen mustard Prednisone	20	7½ years. Dead

Recently, 4 further complete remissions—3 lasting 1 year and one 6 months—have been achieved with actinomycin D, alone in 3 patients, plus surgery in 1.

Forty-two of the 65 patients with complete remissions shown in Table I had lung metastases and one patient had metastases elsewhere; in 22 instances the sites of metastases were not stated.

Five long-term remissions have been reported in men with metastatic choriocarcinomas. Actinomycin D was used in four of these cases, in combination with chlorambucil in two and with chlorambucil and methotrexate in the other two; a combination of vincristine, methotrexate and melphalan was used in the fifth patient.

There was only one patient with a teratocarcinoma without specified embryonal elements (teratoma intermediate A) whose metastases were reported as having regressed completely after chemotherapy (Ansfield *et al.*, 1969). The site of metastatic disease was not given, and at the time the report was made the patient was still being treated with methotrexate, chlorambucil and actinomycin D, duration of remission being then 10 months.

It is, however, with the embryonal carcinomas of the testis (teratomas intermediate B and teratomas anaplastic) that chemotherapy has been most effective in achieving complete remissions. In one report (Kennedy, 1970) the histology relating to 9 out of the 11 successfully-treated patients is not clearly stated, but the text and the probabilities both suggest that these 9 were embryonal carcinomas (Table I). Table II shows the duration of complete remission in 50 (or 59) patients with embryonal carcinoma of the testis. Kennedy used mithramycin alone as his chemotherapeutic agent and all 11 of his successes have been included in Table III which gives the duration of remissions in relation to the drugs successfully used alone.

When the complete remissions achieved by combination chemotherapy—which includes the B drugs (Table IV)—are seen against the remissions achieved by the A drugs alone (Table V), the value of actinomycin D and methotrexate becomes clear. It must of course be remembered that certain combinations have been used much more frequently than others, particularly actinomycin D, methotrexate and chlorambucil. Nitrogen mustard appears in 3 of the successful combined-drug treatments, twice with methotrexate and once with actinomycin D. However, an early report (Ankenman and Balfour, 1961) of chemotherapy for testis tumours gave an account of 1 patient with regression of widespread pulmonary metastases from an embryonal carcinoma after nitrogen mustard alone; a solitary metastasis remained, which was perhaps differentiated as the patient was alive and well 2 years after treatment. If this were accepted as a complete remission—it being the only one due to an alkylating agent used alone—then nitrogen mustard would move into the A drug category.

Royal Marsden Hospital Experience.—Because of severe reactions, the original Memorial Hospital triple-drug therapy (Li *et al.*, 1960) was soon given up in favour of actinomycin D or methotrexate used either alone or in combination with testosterone. The one long-term remission obtained in the patients treated in 1960, 1961 and 1962, followed the use of testosterone. Methotrexate was given at the start of treatment with the testosterone, which was continued because a large abdominal mass was slow to regress with irradiation. A slowly-enlarging rounded shadow, presumed to represent a lung metastasis, was found 5 years later, soon after the testosterone was stopped, and this also regressed slowly but not completely over a period of more than a year when the testosterone was started again. The patient has some static shadowing still present at this site 5 years after the metastasis was first suspected. Like the irradiated abdominal mass causing marked lateral displacement of the left ureter, the lung metastasis regressed extremely slowly and not completely, so although the patient remains alive and well the testosterone effect must be regarded as uncertain.

Lymphography was first used in this hospital in 1962 (Macdonald and Wallace, 1965) and at the same time treatment for patients with tumours of the testis was begun on the 6 MeV linear accelerator (Smithers and Wallace, 1962; Smithers *et al.*, 1971). All patients with tumours of the testis have been staged and irradiated as described in those papers. Patients with metastatic disease already beyond the lymph nodes when first seen or who developed widespread recurrence after irradiation have been treated with chemotherapy. Those with localised recurrence have been treated surgically or by irradiation, with or without chemotherapy. Twenty-one patients with tumours of the testis have been treated with chemotherapy since 1962 by other members of the staff: 3 teratomas intermediate A, 10 intermediate B, 2 anaplastic, 3 trophoblastic and 3 seminomas. One of the intermediate B's has had a complete remission; an account of this patient will be published elsewhere (Bloom, 1971). Dr Bloom was the first to add Provera to the treatment in these cases. This paper, however, deals only with those patients treated under my care in the joint testicular tumour clinic run in association with my colleague Mr D. M. Wallace.

Personal Series.—Chemotherapy has been used in 5 patients with seminomas but in none was there any certainty that the response was due to this treatment alone. One patient died after

15 months with uncontrolled widespread metastases, but all known metastatic tumour was irradiated in the 4 survivors, all of whom have remained free from any detectable recurrence, 3 for over 7 years and one for 2 years and 9 months.

Teratoma Intermediate A.—The results of surgery and radiotherapy for these patients in the early stages are good (80 per cent 2-year recurrence-free rate, Smithers *et al.*, 1971) but our experience confirms that gathered from the literature, namely that when these tumours do disseminate they respond little if at all to our present chemotherapy régimes. In 5 patients in this group, actinomycin D with or without testosterone or Provera, bleomycin, and quadruple-drug therapy with vincristine, nitrogen mustard, Natulan and prednisone have been tried, but there was no complete remission and all these patients died within a year.

Teratoma Intermediate B.—These tumours should perhaps be included with the anaplastic teratomas since the 2 groups correspond fairly closely to the embryonal carcinomas of the American classification and so are likely to be reported as such in United States publications.

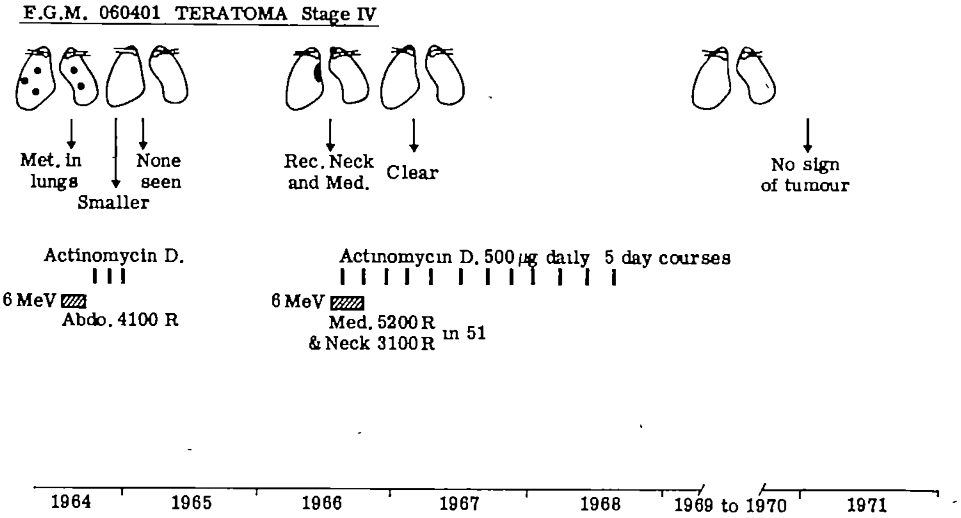


FIG. 1.

Treatment of a patient with multiple lung metastases from a teratoma intermediate B.

Seven patients are in this category, 3 having remissions after actinomycin D alone; in 1 patient these lasted for 2 separate periods of 2½ and 3 months, in one the remission has been maintained for 7 years (Fig. 1) and in the third the lungs have been clear of visible metastases for 1 year.

Teratoma Anaplastic.—These tumours have not only responded best to chemotherapy but have also been those most liable to undergo maturation (Smithers, 1969). When a complete remission is obtained, it would seem that the treatment should be persisted in, perhaps for as long as 2 years; however, if chemotherapy seems to have been stopped too soon, the situation may yet be retrieved, though perhaps the reprieve was due to mediastinal and neck irradiation in one patient (Fig. 1). There is some evidence from experience with Hodgkin's disease to suggest that when localised tumour remains after a good response to chemotherapy by most of the disseminated disease, this may disappear on irradiation, with the patient remaining well thereafter without further treatment. However, we know that with teratomas of the testis chemotherapy may be stopped and no residual tumour or further recurrence requiring treatment may be observed even in patients who have had extensive pulmonary metastases. In one patient a single rounded shadow in the left lower lobe persists; it may well represent a differentiated metastasis but, perhaps wisely, he refuses to have it removed for biopsy (Figs. 2 and 3).

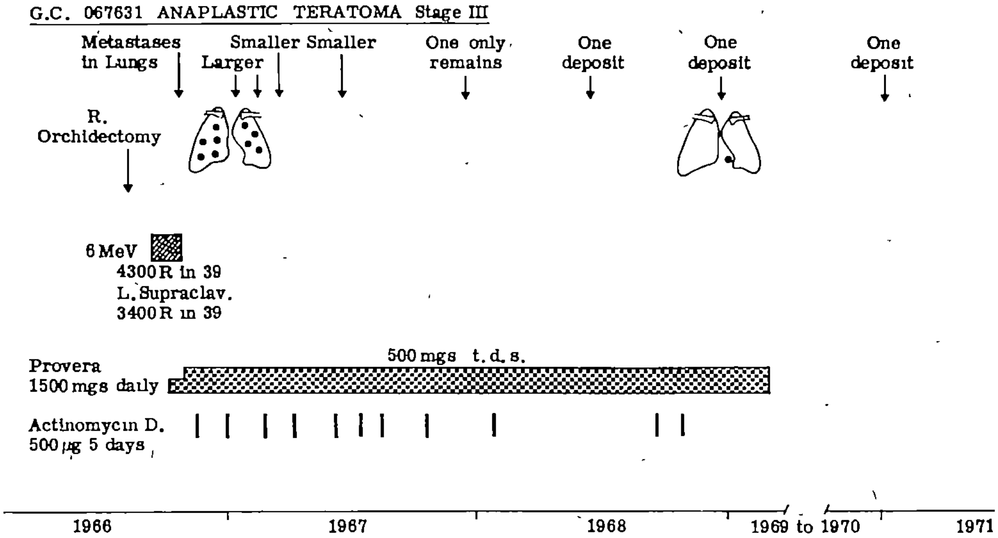
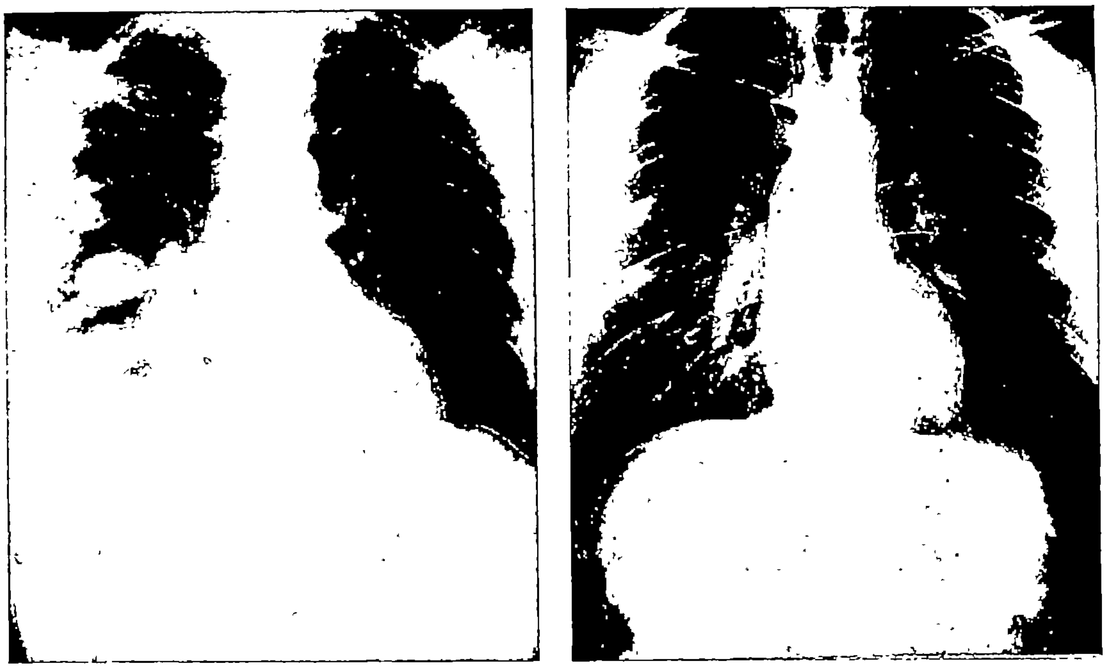


FIG. 2

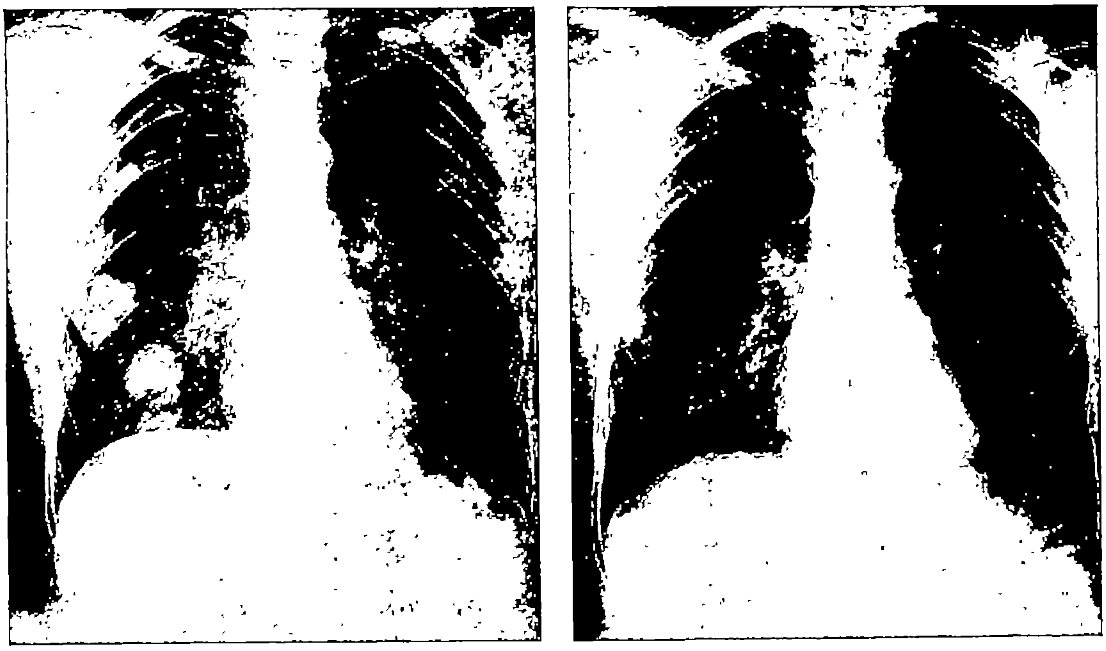
Treatment of a patient with multiple lung metastases from an anaplastic teratoma.



A FIG. 3 B

A, February 1967: lung metastases beginning to regress after third course of treatment in patient shown in Figure 2. B, August 1970: one static deposit remains behind the heart shadow nearly 2 years after the last course of actinomycin D. No other metastases are seen.

There were 18 patients with embryonal carcinomas in the group treated by chemotherapy in the period 1962-67. These are referred to in Table VI, particulars of 6 patients being given in greater detail. Lung metastases responded to chemotherapy in patients 1, 2 and 3; in patients 1 and 2, remissions are still maintained; in patient 3, 2 good but temporary remissions of 2½ and 3 months were obtained with chemotherapy in the midst of repeated irradiation. Patients 4 and 5 had surgical removal of residual masses which had differentiated, chemotherapy having first been given; an account of these has already been published (Smithers, 1969). Patient 6 had a long interval from first treatment to detection of recurrence—well beyond the usual maximum of 2 years—but the recurrences which had been present for an uncertain time in neck and lung when removed surgically 4½ years after first treatment, were both found to be differentiated. A little over 1½ years later, multiple rapidly-growing lung metastases appeared; good, though partial, regression was obtained, first with actinomycin D combined with hormones and later, when this failed, was obtained again with vincristine, nitrogen mustard, Natulan and prednisone. Regression was never complete, however, and the patient died 10 months after starting chemotherapy. Three more recently treated patients have had regression of all visible lung metastases, two for 1 year and one for 6 months on actinomycin D alone.



A FIG. 4 B

A, January 1971: before treatment for lung metastases from an anaplastic teratoma. B, August 1971: regression of metastases. A good response was seen after the second course of treatment.

Some chemotherapy responses are slow to appear. For example, one of the best results has been achieved in a patient whose lung metastases showed no sign of reduction in size until after the third course of actinomycin D was given (Fig. 2). Others are more rapid: in 1 patient regression started with the first course and after 3 courses of actinomycin D no sign of lung metastases remained and the treatment was stopped, it seems prematurely (Fig. 1). In patients responding well, good regression is usually seen after the second course of treatment (Fig. 4). However, one of the complete remissions reported in the literature followed a mere 6 days treatment with methotrexate and the patient was reported to be still free of disease 8 years afterwards (Wyatt and McAninch, 1967).

There is no evidence from any of the joint clinic patients that Provera has added anything to the effect of chemotherapy. The place of testosterone may be more interesting but is not very convincing on the basis of one success uncertainly related to the hormone treatment.

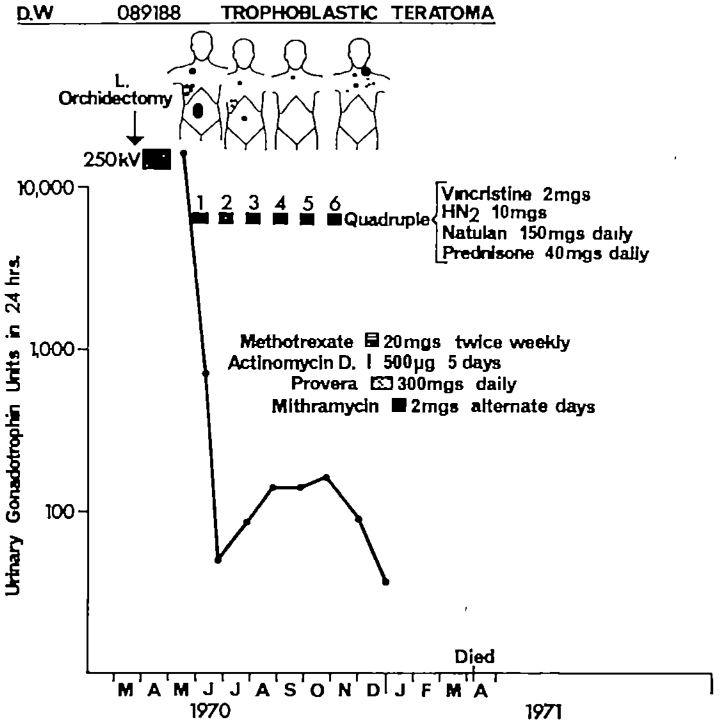


FIG. 5

Treatment of a patient with an abdominal mass and multiple lung metastases from a trophoblastic teratoma.

Teratoma Trophoblastic.—The results of treatment of the pure trophoblastic teratomas have been uniformly disappointing although temporary responses have been achieved with marked reduction in gonadotrophin output in 2 out of 4 patients; Fig. 5 shows such a response in one patient who has recently died.

DISCUSSION

Data on the chemotherapy of teratomas of the testis have been obtained from a critical study of the literature and 65 well-documented examples of complete remission after chemotherapy of metastases from tumours of this type have been accepted.

There has been a disappointing lack of success with the more well-differentiated tumours (teratocarcinomas, teratomas intermediate A) once they have metastasised beyond the lymph nodes. The histology of the case report of a solitary success should be reviewed. It is fortunate that the success-rate with these tumours in the earlier stages is so high.

While complete regression of choriocarcinomas of the testis (teratomas trophoblastic) is infrequent, it does seem to be lasting when it is achieved. Four patients reported to be living at 92, 85, 42 and 35 months and one who died at 64 months after chemotherapy for metastases (Mackenzie, 1966; Solomon *et al.*, 1967; Ansfield *et al.*, 1969), is a real achievement in a difficult group and one which we have so far been unable to emulate.

The disseminated embryonal carcinomas of the testis (teratomas intermediate B and anaplastic) are those most responsive to chemotherapy. Of these, one or two may undergo spontaneous maturation, passing from malignant to benign neoplasia (Smithers, 1969) but the main success in their treatment has been undoubtedly achieved by chemotherapy. A review of the literature and our own experience suggests that the outstanding drugs in obtaining this success have been the antitumour antibiotics. Mithramycin has achieved the largest number of successes when used alone but actinomycin D in combination with other drugs has been concerned in a larger number of complete remissions. The dangers of mithramycin are such that it should only be used by those with considerable experience; kidney damage or unexpected sudden hæmorrhage even in the face of a normal blood-count may occur despite the reduced toxicity of Kennedy's alternate-day régime.

Vincristine has not been used alone often enough for us to find out whether it may qualify for inclusion in the A drug group with vinblastine. Other B drugs are of doubtful value for teratomas of the testis. It is probable that methotrexate has been undervalued, for it has had two successes when used alone and appears in many of the successful combinations, in 8 of which it was the only A drug. The effects of nitrofurazone and hydroxyurea still need to be evaluated. We must certainly look for new ways of tackling metastatic spread in cases of teratocarcinoma (teratoma intermediate A). The available evidence suggests that while the alkylating agents can be useful for seminomas, they may be of little value for the teratomas: a review of the literature shows that, with one possible exception, none have been successful when used alone and that in combination there have only been complete remission when other drugs of known value have been included.

With the embryonal carcinomas of the testis we have so far preferred to use actinomycin D as the drug of first choice (500 micrograms daily for 5 days in repeated courses), often in combination with hormone therapy, and if possible to persist with this, even when response is slow (Figs. 1 and 2). In cases where there is no apparent regression, where the tumour is advancing rapidly, or where recurrence appears after a chemotherapy remission, we now change to mithramycin. For those tumours and situations in which we have so far had little success, we are trying courses of fresh A-drug combinations.

SUMMARY

Chemotherapy for metastatic teratomas of the testis has met with considerable success. Sixty-five examples of complete remission after chemotherapy have been accepted from the published accounts, but many others have been omitted from this review because of inadequate information about the completeness of regression, duration of remission, histology, or drugs used. Of these 65 patients, 25 have had complete remissions lasting for more than 2 years and 11 for more than 5 years at the time of reporting. Four other patients with complete remission, 2 surviving for more than 2 years after treatment for their metastases, are reported here for the first time. The great majority of these patients whose metastases have been treated effectively by chemotherapy have had the more malignant teratomas of the testis, corresponding to those classified as embryonal carcinomas by the U.S. Armed Forces Institute of Pathology. The most successful drugs have been mithramycin, actinomycin D and methotrexate, whether used alone or in combination with other drugs.

Dr Noel Wallace was concerned with the treatment of the early group of patients reported here, and Dr G. Hamilton Fairley and Dr T. J. McElwain with those treated over the last 2 years. I am most grateful to them for their help and advice, particularly to Dr Noel Wallace who did so much to get this project started. In sifting the literature for acceptable data which we could tabulate, I have been assisted by Miss J. B. E. Thompson; we hope that our survey has brought to light most of the useful reports of complete remission of metastatic teratomas of the testis after chemotherapy.

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British Journal of Urology (1972), **44**, 229–234

ELECTRON MICROSCOPY OF THE PRIMARY OBSTRUCTIVE MEGAURETER

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WILLIAMS and Hulme-Moir (1970) have defined the primary obstructive megaureter as a dilatation of the ureter in all but its terminal segment without obvious cause and without vesico-ureteric reflux on micturition. The dilated ureter shows hypertrophied actively peristaltic musculature and whilst the abnormal segment is reduced in calibre it will permit the passage of a probe. No mucosal valves are present. This paper outlines an electron microscopic study of the narrow segment in an attempt to define the cause of the obstruction.

The results of electron microscopical studies of the innervation and musculature of the normal human ureter have been presented in earlier papers (Notley, 1968, 1969 and 1970*a*) and these observations have provided the structural evidence necessary to support an hypothesis describing the mechanism of ureteric peristalsis (Notley, 1970*b*). Close contacts between ureteric muscle cells were demonstrated which are similar to the nexuses found in other organs (Dewey and Barr, 1964) and shown to transmit electrical activity from one cell to another (Barr, Berger and Dewey, 1968). Peristalsis commences in the pelvi-ureteric segment of the ureter when it is distended with urine; electrical activity arising here dominates the whole ureter (Bozler, 1938) and spreads from muscle cell to muscle cell along the ureter by way of the close contacts to produce the co-ordinated wave of ureteric peristalsis, a nerve network not being involved.

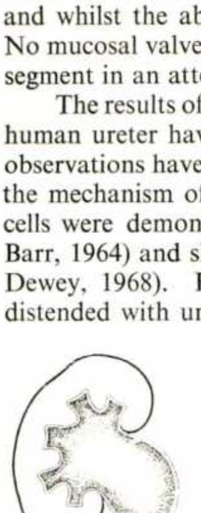

FIG. 1

Diagram illustrating obstruction at the pelvi-ureteric segment in idiopathic hydronephrosis due to excess collagen in submucosa and muscle layer.

It has been suggested (Campbell, 1970) that obstructive megaureter is analogous to situations in the intestinal canal, such as Hirschsprung's disease and achalasia of the cardia, where there is a failure of motility in an aganglionic segment producing a functional obstruction (Bodian, Stephens and Ward, 1949; Ellis, 1962). However, Campbell's comments seem to be based on a too liberal interpretation of the findings of Swenson, MacMahon, Jacques and Campbell (1951, 1952) in certain patients suffering from Hirschsprung's disease who also had a dilated urinary tract. The problem of identifying autonomic ganglia with the optical microscope are well known (Richardson, 1960) and have been discussed in relation to the innervation of the ureter (Notley, 1971), where no ganglion cells can be found with the electron microscope. Whatever the cause of obstructive megaureter it cannot be neuromuscular inco-ordination due to defective ganglia. Other possible ætiological factors reported are a predominance and hypertrophy of circularly orientated muscle fibres in the narrow region (Hutch and Tanagho, 1965) or a total muscular defect with a resulting failure in conduction of peristalsis across this part of the ureter (Mackinnon, Foote, Wiglesworth and Blennerhassett, 1970).

The obstructive megaureter has much in common with idiopathic hydronephrosis, both having a narrow segment of ureter offering sufficient functional obstruction to produce dilatation of the proximal system. An ultrastructural study of the pelvi-ureteric segment below idiopathic hydronephrosis has demonstrated abnormally large amounts of collagen in the muscular layer and the lamina propria (Notley, 1968 and 1970*b*). This inelastic segment is probably responsible for the development of hydronephrosis by preventing the expansion of this part of the ureter necessary to accommodate the extra load during diuresis (Fig. 1). This investigation was undertaken to see if a similar lesion is present in the narrow distal segment of the obstructive megaureter.

Materials and Methods.—The narrow segments of 8 obstructive megaureters have been examined, 6 from children and 2 from adults. In each case a distinct narrow segment was demonstrated at operation before reimplanting the shortened and tapered ureter into the bladder by the Politano-Leadbetter technique (1958). The narrow segments were opened longitudinally so that blocks of tissue 0·75 mm. wide could be cut through the whole thickness of the ureteric wall. Blocks from the whole circumference of the ureter were taken and immersed in ice-cold fixative, either 1 per cent Millonig's osmium tetroxide solution or 3 per cent glutaraldehyde in phosphate buffer. Two or four hours were allowed respectively for fixation. When glutaraldehyde was used the tissue was transferred to the Millonig's solution after washing in glutaraldehyde washing fluid. After washing and dehydration the tissue was embedded in Araldite resin. Ultrathin sections were cut using a diamond knife on a Porter Blum microtome, stained with lead citrate and uranyl acetate and examined with a Sieman's XIB electron microscope.

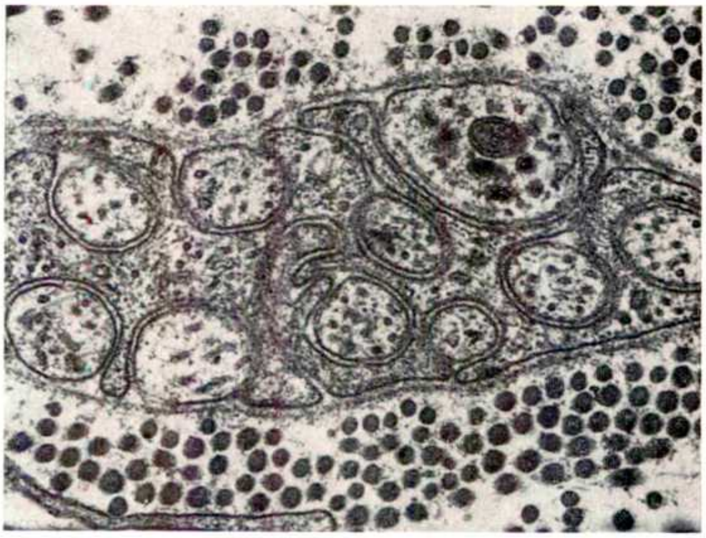

FIG. 2

Nerve bundle lying in close association with blood vessel in ureteric wall. × 40,000.

Results.—The basic structural arrangement of the wall of the narrow segment of the obstructive megaureter is the same as that of the normal ureter. There is an outer adventitia, a muscular layer and an inner mucous membrane, consisting of the transitional epithelium and an underlying submucosa or lamina propria.

The Adventitia.—The adventitia is similar to that of the normal ureter, consisting of many bundles of collagen fibres and blood vessels, many of which receive an autonomic innervation (Fig. 2). Large bundles of unmyelinated nerve fibres are also present.

The Muscle Layer.—The muscular coat is composed of bundles of similarly orientated smooth muscle cells, but the bundles are more widely separated from each other than in the normal ureteric muscle layer by large collections of collagen fibres (Fig. 3). In addition abnormally large numbers of collagen fibres lie between the individual muscle cells in many of the bundles.

This increase in collagen is found throughout the whole length of the narrowed segment as far down as the intramural ureter. The ultrastructural appearance of the muscle fibres is the same as those in the normal ureter and the majority in this region have a longitudinal orientation.

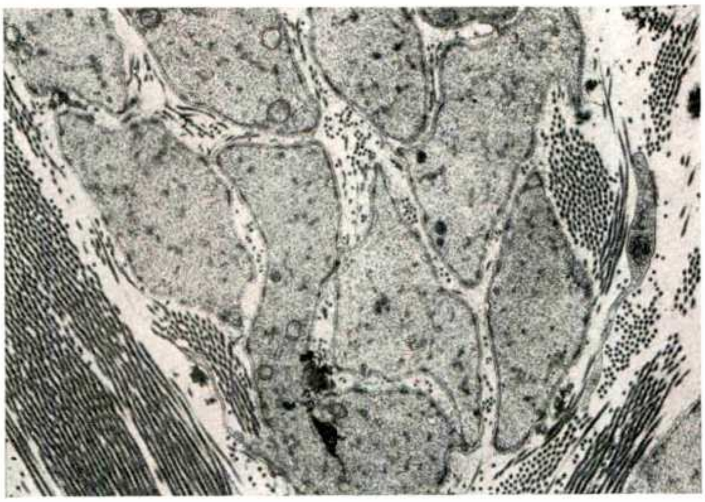

FIG. 3
Muscle bundles widely separated by large numbers of collagen fibres. × 7,800.

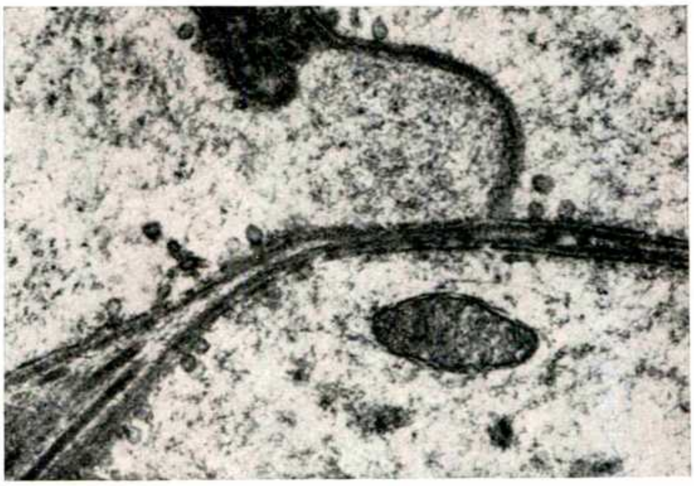

FIG. 4
Close contact between two ureteric smooth muscle cells. × 40,000.

Intimate apposition between the walls of the individual muscle fibres is frequent (Fig. 4). At these contact points the basement membranes of the muscle cells involved become fused so that the cell plasma membranes lie close together. As in the normal ureter these areas of close apposition may take various forms, the cell walls may be interdigitated or a process from one cell may reach out to the neighbouring cell. The plasma membranes lie about 200 Å apart at these points.

Many bundles of unmyelinated nerve fibres are scattered throughout the whole thickness of the muscular layer. Some supply the blood vessels in this region, but many others lie between the bundles of smooth muscle cells or amongst individual cells. In the latter situation some of the axons display the characteristics of terminal nerve areas and lie in close relationship to the muscle cells (Fig. 5).

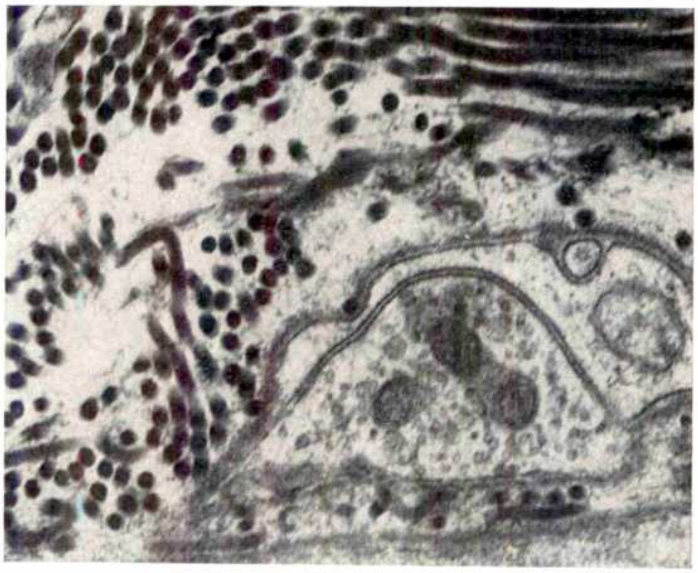

FIG. 5

Small bundle of unmyelinated nerves lying close to ureteric smooth muscle cells. ×41,000.

The Submucosal Layer of the Mucous Membrane.—This layer is very considerably expanded throughout the whole extent of the narrow segment of the obstructive megaureter in comparison with the normal ureter. Vast numbers of collagen fibres lie close together, running in all directions enclosing fibrocytes and small blood vessels. Numerous bundles of unmyelinated nerve fibres are present in this layer, as in the normal ureter, with many axons showing typical terminal areas.

DISCUSSION

It is clear that the obstructive megaureter has no common ætiology with achalasia of the cardia or Hirschsprung's disease of the colon as autonomic ganglia are not a feature of normal ureteric anatomy.

This study demonstrates normal autonomic innervation to the ureteric muscle cells and the blood vessels of the narrow segment with normal connections between the muscle cells. In this respect there is no difference from normal ureter and peristaltic waves would be expected to pass normally through this segment. The electron microscope reveals no excess of circular muscle fibres, indeed it seems that if there is any predominance longitudinal fibres are in a small majority. There is, however, an enormous increase in the amount of fibrous tissue in the part of the ureter, with greatly increased numbers of collagen fibres in the lamina propria and in between the ureteric muscle cells. Similar findings have been reported by Gregoir and Debled (1969). This excess of collagen must reduce the distensibility of the ureter in this narrow region so that during diuresis the rate of flow of urine into the bladder cannot increase in proportion and dilatation of the proximal ureter will tend to occur (Fig. 6). The proximal ureter must work harder to overcome the high outflow resistance if it is to achieve any increase of flow of urine into the bladder at all during diuresis; consequently its muscular wall will hypertrophy and its intraluminal pressure might be expected to rise.

These observations suggest that the anatomical abnormality in the narrow distal segment of the obstructive megaureter is the same as in the narrow pelvi-ureteric segment below idiopathic hydronephrosis, an increased amount of collagen in the lamina propria and in the muscular layer, but why this situation should exist is quite unknown. It is peculiar that this situation is seen only at these two sites and not in mid ureter. Both conditions can be successfully relieved by excision of the narrow segment followed by restoration of continuity of the collecting system. When the condition is of long standing the structural changes which have occurred in the proximal ureter and pelvis as a result of obstruction will not regress and dilatation may remain although the obstructing lesion has been removed.

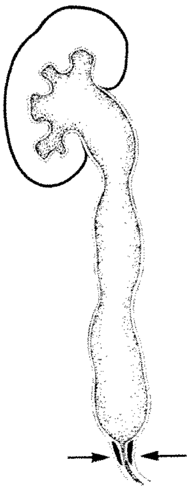

FIG. 6
Diagram illustrating obstruction at the terminal segment of the obstructive megaureter due to excess collagen in submucosa and muscle layer.

SUMMARY

The ultrastructure of the narrow segment of the obstructive megaureter has been studied. The muscle cells are normal in appearance, their connections with each other are present in normal form and number and they receive a normal autonomic innervation. As in normal ureter no ganglion cells have been found.

A great increase in the amount of collagen fibres in the submucosa and the muscle coat has been demonstrated which it is suggested is responsible for the poor drainage of the ureter and its consequent dilatation. This lesion is similar to that demonstrated in the narrow pelvi-ureteric segment of idiopathic hydronephrosis. The ætiology in either situation is obscure.

I am most grateful to Mr D. Innes Williams for providing the material for this study. My thanks are also due to Professor F. R. Johnson of The London Hospital, Professor R. Warwick of Guy's Hospital and Professor R. M. H. McMinn of the Royal College of Surgeons for their assistance and the use of their technical facilities.

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ORAL ADMINISTRATION OF A NEW CARBENICILLIN IN THE TREATMENT OF URINARY TRACT INFECTION

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CARBENICILLIN has a broader bactericidal spectrum against Gram-negative bacteria than other available penicillins (Brumfitt, Percival and Leigh, 1967). Of particular interest is its activity against *Pseudomonas æruginosa* and against both lactamase and non-lactamase producing strains of *Proteus rettgeri, P. morganii,* and *P. vulgaris*. To date the drug has been restricted to parenteral administration because of its poor absorption when administered orally. Recently the indanyl ester of carbenicillin (6-(2-phenyl-2-5-indanyloxycarbonyl)) acetamido penicillanic acid) has been shown to be acid stable and absorbed when given orally (Therapeutics Research Division, Pfizer, Limited—personal communication).

We report here a preliminary trial to assess the effectiveness of the carbenicillin ester (CP 15464) in eradicating urinary tract infection from women with a radiologically normal urinary tract and normal renal function.

Patients and Methods.—27 non-pregnant women between the age of 18 and 45 years who presented with a symptomatic or an asymptomatic urinary tract infection were treated with the carbenicillin ester. Patients with impaired hepatic function, a history of penicillin allergy or a serum creatinine exceeding 1·2 mg. per 100 ml. (Autoanalyser-N Methodology) were not considered for the trial. Only women with a radiologically normal urinary tract were admitted to the study. The diagnosis of urinary infection was made by culturing bacteria from a specimen of urine obtained by suprapubic bladder aspiration (Bailey and Little, 1969). The sensitivity of each infecting organism was assessed using sensitivity discs containing 100 mcg. carbenicillin (Oxoid). Before treatment, every woman had blood taken for estimation of hæmoglobin, differential and total white cell count, erythrocyte sedimentation rate and the serum levels of alkaline phosphatase, urea, creatinine, glutamic oxaloacetic transaminase and glutamic pyruvic transaminase.

All patients received 1 gram of the carbenicillin ester by mouth every 6 hours for 7 days. One week after the end of the course of treatment a further specimen of urine was taken either by the midstream or suprapubic technique to check on bacteriological cure. If the repeat urine specimen was obtained by the former method and contained in excess of 10,000 pathogenic organisms per ml. a specimen was taken by suprapubic aspiration to make a conclusive diagnosis. If the latter specimen was infected the patient was considered a treatment failure and excluded from further assessment in this study. If the patients were initially symptomatic they were assessed for clinical improvement. The presence of side-effects while taking the drug was enquired for by asking each patient the following question: " Did the tablets upset you in any way? " The above hæmatological and biochemical parameters were repeated 1 week after finishing the course of treatment.

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The women with sterile urine 1 week after treatment were given no further medication and reviewed again 6 weeks after finishing treatment. Urine was again taken for culture as above. At this time, the assesment of the drug was considered complete.

Results.—The organisms responsible for the urinary tract infection are shown in Table I. All bacteria were sensitive to carbenicillin on *in vitro* testing. One further patient with acute pyelonephritis due to *Escherichia coli* (*E. coli*) was excluded from the trial after 36 hours treatment as the organism was found to be resistant to the drug on *in vitro* testing and the patient was showing no signs of clinical improvement.

TABLE I

Results of Treatment Related to Infecting Organisms
(1 Week after Course of Treatment Finished)

Original Organism	Total No.	No. Eradicated	No. with Similar Organism or same Serotype of *E. coli*	No. with Different Organisms
E. coli	20	14	2	4
Coagulase negative staphylococcus	3	1	1	1
Proteus mirabilis	2	0	1	1
E. coli and coagulase negative staphylococcus	2	1	1 (*E. coli still* present)	0
Total	27	16 (59%)	5	6

TABLE II

Results of Treatment Related to Presenting Clinical State
(1 Week after Course of Treatment Finished)

Clinical State	Total No.	No. with Sterile Urine	No. with Similar Organism or same Serotype of *E. coli*	No. with Different Organism
Symptomatic-acute pyelonephritis	4	3	1	0
Symptomatic-cystitis	14	8	3	3
Asymptomatic	9	5	1	3
Total	27	16 (59%)	5	

The presenting clinical state of the 27 women in the trial is included in Table II.

When the urine of each woman was cultured 1 week after the end of the course of treatment 16 (59 per cent) of the specimens were sterile (Tables I and II). All the patients who were initially symptomatic and whose urine was sterile at this stage were also free of symptoms. Six women were infected with a different organism or a different serotype of *E. coli* (3 resistant to carbenicillin) 1 week after finishing treatment. The remaining 5 women were infected with a similar organism or the same serotype *E. coli*. One of the 2 women with a mixed infection (Table I) had only the coagulase negative staphylococcus eradicated from the urine while the same serotype of *E. coli* was again cultured.

TABLE III

Results of Treatment Related to Presenting Clinical State
(6 Weeks after Course of Treatment Finished)

Clinical State	Total No.	No. with Sterile Urine	No. with Different Organism
Symptomatic-acute pyelonephritis	3	3	0
Symptomatic-cystitis	8	7	1
Asymptomatic	5	3	2
Total	16	13	3

TABLE IV

Side-effects During Treatment

Side-effects	No.
After taste, indigestion, heartburn nausea	3
Vomiting—once only	2
—troublesome	1
Diarrhœa—mild (in 1 occurred 3 days after end of treatment and associated with abdominal discomfort)	5
—troublesome	2
Constipation and flatus	1
Tiredness	1
Mild skin rash (on 7th day of treatment)	1
Fever (in 1 associated with sore throat)	2
Vulvovaginitis	1
Nil	14

Of the 16 women with sterile urine 1 week after completing the course of treatment, 3 were infected with a different organism or a different *E. coli* serotype (1 resistant to carbenicillin) 6 weeks after treatment was completed (Table III).

The side effects attributed to the drug are shown in Table IV. The treatment of one woman was terminated after 5 days because of troublesome diarrhœa, occasional vomiting and fever. The urinary infection of this patient had been successfully eradicated by this time. Fourteen women noted no adverse effects. None of the hæmatological or biochemical parameters which were estimated deviated from normal during the course of treatment.

DISCUSSION

Brumfitt *et al.* (1967) found that the important property of the semisynthetic penicillin, carbenicillin, was its wider spectrum against Gram-negative bacteria than either ampicillin or cephaloridine. This applied particularly to *Ps. æruginosa* and *Proteus spp* other than *P. mirabilis*. These authors also found parenteral carbenicillin effective in the treatment of severe infections by hospital strains of *E. coli* which were resistant to ampicillin and cephaloridine. The main disadvantages of carbenicillin compared with other penicillins was its failure to be absorbed from the gut and that the intramuscular injection was painful.

We report here a clinical study using an acid stable indanyl ester of carbenicillin which is absorbed when given orally. Twenty-seven women with a symptomatic or an asymptomatic urinary tract infection were treated with this oral preparation of carbenicillin. All had a radiologically normal urinary tract and normal renal function. Sixteen of these 27 patients were cured clinically and bacteriologically after completing a 1-week course of treatment. Our results show that carbenicillin can be effective in the treatment of urinary infection when it is given orally in the ester form.

These results with the carbenicillin ester are similar to our own unpublished observations and to those of some other groups (Reeves, Faiers, Pursell and Brumfitt 1969; Bieder and Little, 1970; Charlton, O'Grady, MacSherry, and Sutcliffe, 1970; Davies, Strangeways, Mitchell, Beilin, Ledingham and Holt, 1971) when using other penicillins such as ampicillin or cephalosporins such as cephalexin, in similar, but not identical clinical situations.

The failure to eradicate the infecting organism in some of the women reported here could possibly be due to the production of spheroplasts within the urinary tract, which is likely when using antibiotics such as the penicillins or cephalosporins which interfere with bacterial cell wall biosynthesis.

The majority of side-effects observed with the carbenicillin ester were referable to the gastro-intestinal tract with mild diarrhœa predominating. The nausea, heartburn and after taste could probably be reduced by improving the coating of the preparation. This will be important particularly when doses in excess of 4 g. daily may be required.

Most of the antibiotic in serum exists as carbenicillin although small quantities of CP 15464 are also present for a few hours after administration. Since carbenicillin itself is poorly absorbed it can be concluded that most of the CP 15464 remains intact in the gut long enough for intestinal absorption to occur. After absorption, the ester is rapidly hydrolysed to carbenicillin and excreted in this form. Indanol, the other moiety produced upon hydrolysis of CP 15464, can also be found in low concentration in the serum, where it exists as the free compound or as a sulphate ester conjugate. Following cessation of drug administration, serum levels of indanol decline rapidly with a half-life of less than 24 hours, much of it being excreted by the kidneys. Extensive animal work has shown no evidence of harmful effects.

In patients with normal renal function the serum levels of carbenicillin obtained following 1 g. of the ester administered orally (Therapeutics Research Division, Pfizer Limited—personal communication) are equivalent to those reached following 0·25 g. of carbenicillin given by the intramuscular route (Knudsen, Rolinson and Sutherland, 1967).

In our study we have shown that the new preparation of oral carbenicillin is effective in treating urinary tract infection but we have only covered a small area of the wide bacteriological spectrum of carbenicillin. However in addition, we have successfully eradicated *Ps. æruginosa* from the urinary tract of a 30 kg. boy with one remaining kidney which is drained by a nephrostomy and has a creatinine clearance of 10 ml./min. This patient received 0·5 g. of carbenicillin ester 6-hourly for 1 week after previous courses of treatment with gentamicin and colistin had failed to eliminate the organism.

Further studies with this oral preparation and trials in different clinical situations appear warranted. Of particular interest would be an assessment of the drug in patients with urinary infection in the presence of renal functional impairment with or without an abnormal urinary tract, in combination with other antibacterial agents, and in the treatment of bacterial infections outside the urinary tract.

SUMMARY

Oral administration of carbenicillin indanyl ester in a dose of 1 gram six-hourly for 7 days has proved successful in eradicating urinary infection from 16 of 27 women with a radiologically normal urinary tract and normal renal function. The drug was free from serious side-effects although mild gastro-intestinal symptoms were not infrequent. Further clinical trials would seem justifiable.

We wish to thank Mr A. P. Roberts for his constructive criticism and helpful advice, and Mr A. Waterman and Miss C. Fitzpatrick for technical assistance. We are also grateful to Dr K. Budd and Dr R. B. Vaughan of the Clinical Research Department, Pfizer Limited, Sandwich, Kent, for their assistance in formulating the protocol and for providing supplies of CP 15464. Reprint requests to K.G.K.

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KIDNEY PRESERVATION: CRYO-PRECIPITATED PLASMA PERFUSION AND THE PROGRESSIVE OSMOTIC EFFECT

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IN a previous paper (Chapman, 1971) it has been shown that progressively increasing the osmolality of a simulated intracellular fluid perfusate by repeated additions of dextrose enhances the preservation of function in the canine kidney on hypothermic perfusion for 24 hours. Undoubtedly the best method of donor kidney preservation published to date is by perfusion with cryo-precipitated plasma (Belzer *et al.*, 1968; Belzer and Kountz, 1970). This is borne out by our own experiences with this technique and with synthetic perfusates. In view of the previous findings in this laboratory it was decided to explore the effect of progressively increasing the osmolality of cryo-precipitated plasma perfusate on 24-hour preservation of canine kidneys.

Most previous investigations of renal preservation have relied on prolonged survival of the animal into which the preserved organ has been transplanted as the criterion of success. Measurements of functional capacity have usually been restricted to the capacity of the organ to reduce a raised serum creatinine and blood urea nitrogen in the days and weeks following transplantation. We have attempted to provide a more sensitive quantitation of the degree of successful preservation by measuring both glomerular function and tubular secretory ability in the immediate post-preservation period. This we hope will give a more accurate assessment of the effect of changes in preservation conditions than has hitherto been the case.

Materials and Methods.—The experiments were performed on adult greyhounds, anæsthetised with intravenous nembutal. All animals were destroyed under the same anæsthetic at the end of the experiment. Where 24-hour preservations were performed on consecutive days, the first recipient became the second donor.

In the donor animal, the kidney was approached through a midline incision, the ureter was isolated and divided, the proximal end being catheterised to facilitate urine sampling. Endogenous creatinine clearance and tubular maximum secretory capacity for PAH were then measured over 3 consecutive 10-minute periods, commencing 15 to 20 minutes after the commencement of an intravenous infusion of PAH labelled with I^{131} Hippuran. A meticulous nephrectomy was then performed, the renal artery and vein being clamped simultaneously after the induction of a frusemide diuresis.

The perfusion engine has previously been described (Chapman, 1971). Perfusions were carried out with a pulsatile pressure of 80 mm. Hg 60 mm. Hg at a rate of 120 pulses per minute. The perfusate was oxygenated by being passed through a membrane oxygenator. The perfusate delivered to the organ was maintained at 8°C ± 2°C. All preservations were for 24 hours.

At the end of perfusion the kidney was transferred in perfusate at 5°C with the vessels clamped to the prepared recipient animal, fully heparinised, with cannulæ in the common femoral artery and vein. Restoration of the circulation to the kidney was simply achieved by connecting the appropriate cannulæ (for description of this method see Bartlett *et al.*, 1969). In the ensuing 90 to 120 minutes blood-flow through the organ was periodically measured and endogenous creatinine clearances and Tm_{PAH} were again measured as in the donor situation.

Perfusate.—The perfusate was prepared from pooled human plasma obtained from "out of date" stored blood or removed from units used for "packed cell" transfusions. This was kept in a deep-freeze unit and prepared immediately prior to the experiment according to the method described by Belzer by rapid thawing and filtration through 0·22 μ filters (Millipore Corporation). To each litre of this filtrate was added 5 ml. of 50 per cent dextrose, 80 units of soluble insulin, 100 mg. Hydrocortisone Sodium Succinate, 200,000 units of Benzylpenicillin and 2 ml. 50 per cent Magnesium Sulphate. Belzer (Belzer and Kountz, 1970) described an additional step of diluting his perfusate by the addition of approximately 1/7th the volume of water in order to lower the concentration of sodium to normal values. In our preparation this would have taken the sodium level to the lower limit of normal values and have reduced still further an already very low chloride value, so this step was dispensed with.

In the short period of refrigerator storage that was necessary while the perfusion apparatus was being set up and the donor operation was being performed this preparation usually developed further turbidity and on two occasions a definite coagulum formed which blocked the filter of a commercial intravenous infusion apparatus.

Chemical analysis of the perfusate was performed in each case at the commencement and end of the preservation period and once or twice during each perfusion. The results of the initial analyses are given in Table I.

TABLE I

Mean Initial Values for the Perfusate in all Experiments

Total protein:	55·7	gm. per litre
Dextrose:	8757	mg. per litre
Sodium:	152·4	mEq per litre
Potassium:	10·2	mEq per liter
Magnesium:	11·8	mEq per litre
Chloride:	65	mEq per litre
Phosphate:	55	mg. phosphorus per litre
pH:	7·13	
Osmolality:	307	millio-smols per kilo

Three groups of experiments were performed:

Group A	Controls. Ten kidneys were transferred immediately from their own pedicles to prepared arterial and venous cannulæ in the same animal.
Group B	Six kidneys were preserved for 24 hours using the perfusate as described above without any addition.
Group C	Eight kidneys were preserved for 24 hours using the same perfusate with the addition of 250 mg. dextrose (as 25 per cent solution) per litre of perfusate every 30 minutes.

Results.—*Group A.*—The mean warm ischæmia time in this group was 7 minutes and 12 seconds from the moment of clamping the vascular pedicle to re-establishing the circulation.

For each individual kidney the average of 3 measurements of endogenous creatinine clearance, expressed as a factor of the weight of kidney and the Tm_{PAH}, similarly expressed, were calculated for the *in situ* and the " transplanted " situation. The " transplanted " function was then expressed as a percentage of the initial measurements.

Mean retention of the endogenous creatinine clearance capability in these control kidneys was 51·5 per cent. Mean retention of Tm_{PAH} was 65·4 per cent.

Mean flow on the re-established circulation was initially 2·43 ml./gm. of kidney per minute and 2·85 ml./gm./min. at the end of the experiment, the individual values ranging from 1·08 ml./gm./min. to 4·70 ml./gm./min.

Group B.—The mean warm ischæmia time in this group was 7 minutes and 30 seconds.

Mean preservation of initial endogenous creatinine clearance was 14·85 per cent and mean preservation of Tm_{PAH} was 18·13 per cent.

Mean initial flow on the re-established circulation was 4·2 ml./gm./min. Unfortunately the flow was not measured at the end of the experiment in these cases.

Group C.—Mean warm ischæmia time in these cases was 4 minutes and 45 seconds.

Mean preservation of endogenous creatinine clearance in these cases where the osmolality of the perfusate was progressively raised during the perfusion was 26·75 per cent and mean preservation of Tm_{PAH} was 36·01 per cent. The results obtained in Groups B and C are shown diagramatically in Figure 1.

Mean initial flow on the re-established circulation was 2·95 ml./gm./min. and final flow averaged 3·24 ml./gm./min., with values ranging from 1·82 to 4·80 ml./gm./min.

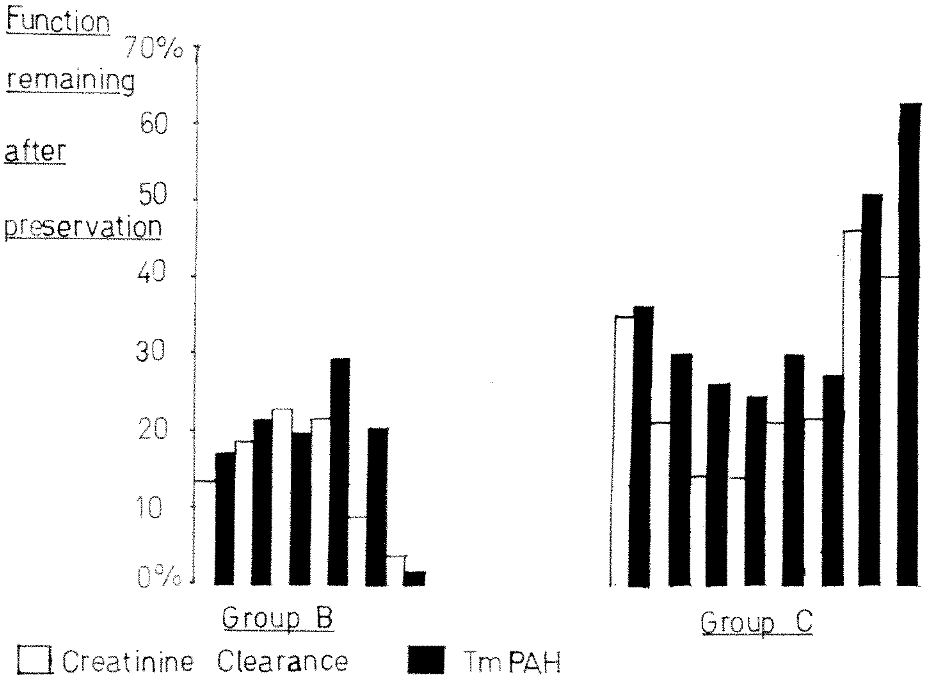

FIG. 1

The results for each kidney are expressed as a percentage of the *in situ* values for the same kidney. Tm_{PAH} and endogenous creatinine clearance for each individual kidney are shown side by side.

Perfusate Changes.—Changes in the perfusate constitution during the course of each experiment were carefully monitored. Total protein, sodium, magnesium and chloride levels did not change significantly in the 24 hours on average, although small increases or decreases were noted in individual experiments. In every experiment both potassium and phosphate increased in concentration, potassium by about 0·6 milli-equivalents per litre (6 per cent) and phosphate, measured as phosphorus, by 12 mg. per litre (20 per cent). These changes are quite small in absolute terms and may not be significant.

In Group B there was a mean net loss of dextrose from the perfusate of 660 mg. per litre. This probably occurred by diffusion of dextrose molecules from the perfusate into the renal parenchymal cells. The mean rise in dextrose concentration was 11,738 mg. per litre in Group C. This corresponded with a net rise in the osmolality of the perfusate in this group of 61 milli-osmols per kilogramme, in the 24 hours.

In all experiments in both series, the pH of the perfusate rose during the preservation period. The major part of this change occurred in the first 3 hours of perfusion. Mean pH at the moment

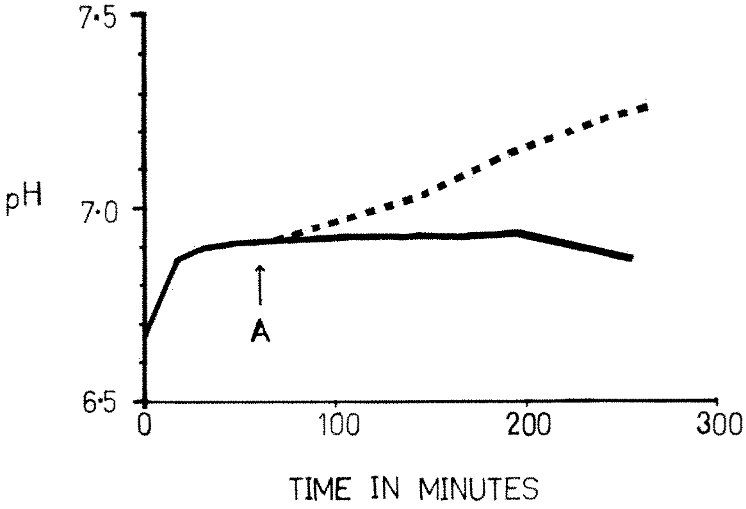

FIG. 2

The interrupted line shows the changes in pH of the perfusate from the moment of commencing flow in the machine, the oxygenator working with a flow of air only. The superimposed broken line shows the subsequent changes from the moment that the kidney to be preserved was connected into the circuit (A). This is a composite graph of 2 separate experiments.

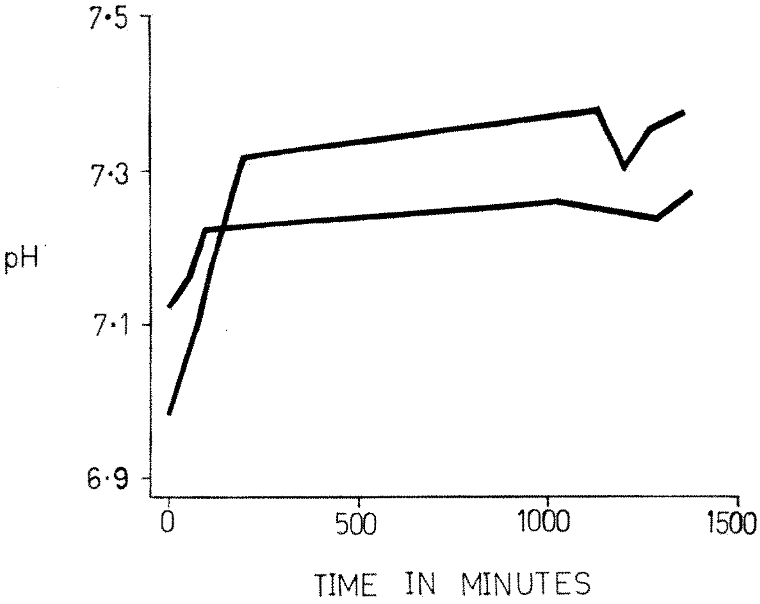

FIG. 3

pH changes throughout two typical preservations, one with and one without dextrose additions. Dextrose tends to produce slight acidification of the perfusate.

when the kidney was attached to the preservation apparatus was 7·13. Mean final pH was 7·32 in Group B and 7·31 in Group C.

The perfusate in our experiments immediately before priming the perfusion engine had a pH varying between 6·68 and 6·95. When the apparatus was run with air only passing through the gas exchanger and no organ in the circuit, the pH changed by approximately 0·20 in the first 30 minutes and then held steady. If the oxygenator was excluded from the system the pH change was much slower but of the same magnitude eventually. The kidney was usually connected after 30 to 60 minutes running time and then the pH rose once more but again less rapidly than in the initial phase (Fig. 2). pH changes recorded in two typical experiments are reproduced in Figure 3.

DISCUSSION

The initial rise in pH probably reflects a loss of carbon dioxide from the plasma. The further change in pH that occurs when the organ is attached to the system may well reflect loss of CO_2 from the renal tissue. The slower rate of this secondary change can be accounted for by the time taken for equilibration of CO_2 tension between the organ and the perfusate. These pH changes can be controlled by passing carbon dioxide through the oxygenator, when the meter readings can be quite nicely titrated against the carbon dioxide flow. No attempt was made to control pH by this means in this series.

Although this is a relatively small series of experiments and the findings cannot be demonstrated to have any high degree of statistical reliability on this count, nevertheless, the observation of enhanced preservation of function by progressive increments in the concentration of dextrose in the perfusate agrees with the findings in one other published series of experiments using a synthetic perfusate containing no colloid fraction (Chapman 1971) and another series, as yet unpublished, in which albumin was added to the perfusate.

Cort *et al.* (1958) suggested that hypothermia alone produces cellular swelling in renal cortical slices. Enerson and Berman (1966) came to the same conclusion using rat diaphragm muscle cells, and further showed that hypoxia exacerbates this swelling, eventually leading to irreversible cellular damage and cell death. Our own findings show that this appears to be true even in the presence of a grossly hypertonic perfusate over a 24-hour preservation period. Using a synthetic perfusate in hypotonic, isotonic and hypertonic forms, similar weight gains occurred in the organs over 24 hours, associated with increasing vascular resistance and deteriorating perfusate flow through the kidney. However, it was noted that hypertonic perfusates gave an initially high perfusate flow rate, but this was not maintained. A plausible explanation of this phenomenon is that osmotic extraction of intracellular water was not maintained because the cell walls are permeable to dextrose molecules, though less so than to the smaller water molecules, and so eventually, but in less than 24 hours, an osmotic equilibrium is achieved. The loss of an average of 660 mg. dextrose per litre of perfusate in the Group B experiments supports the contention that the molecule diffuses into the cells of the kidney. This quantity of dextrose approximates to the total utilisation for metabolism of this substance of a 100 g. kidney in 24 hours at 37°C (calculated on the basis of work on rabbit kidney cortex slices, Lee and Peter, 1969). It is unlikely that anything approaching this quantity could be metabolised at 5°C to 10°C in the same time.

Progressive but small rises in the osmotic capability of the perfusate throughout the period of preservation prevent the achievement of osmotic equilibrium between the cells and the perfusate, giving a perpetual tendency to extract water from the intracellular fluid which counteracts the tendency of hypothermic cells to swelling and eventual disruption.

Cryo-precipitated plasma perfusions show less tendency to weight gain and increasing vascular resistance than perfusions with a synthetic medium in our experience. This is probably due to the presence of some biologically active constituent affecting the integrity of cell membranes or active in some other way in the vasculature of the organ. In the experiments of Group C it was not possible to demonstrate any significant enhancement of perfusate flow attributable to the progressive osmotic effect as has previously been demonstrated using a synthetic perfusate.

SUMMARY

A quantitative assessment of the degree of preservation of kidneys perfused for 24 hours using cryo-precipitated plasma is made in terms of both glomerular filtration rate and tubular function. Preservation by this technique appears to be enhanced by progressively increasing the dextrose content of the perfusate throughout the preservation and its action is ascribed to its osmotic effect.

We would like to express our appreciation to Mr J. E. A. Wickham and Christopher D. Shelton for their help and advice during this work, and to thank the staff of the Blood transfusion and Chemical Pathology Departments of St Bartholomew's Hospital for providing the plasma and help with chemical estimations respectively. This work was aided by a grant from the Joint Research Board of St Bartholomew's Hospital.

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THE LOBAR STRUCTURE OF THE KIDNEY

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FULLY appreciated by comparative anatomists, described in the embryo and infant by human anatomists, the lobar structure of the kidney is still neglected by most clinical disciplines. With the evolution and expansion of nephrology, and the gradual definition or re-definition of kidney disease that has resulted, the clinical implications of the lobar structure are assuming increasing importance. This contribution is an attempt to draw attention to the value of this concept and to add a few original observations.

The " septa " of Bertin.—Perhaps some of the prevalent misunderstanding derives from a misinterpretation which found its way into textbooks of anatomy in the late eighteenth century.

In 1744 the French anatomist Exupere Joseph Bertin read a paper before the Academie Royale des Science in Paris entitled " Memoire pour servir a l'histoire des reins ". In it, among other things, he described in detail the intrusions of cortical tissue between the renal pyramids (Fig. 1). He pointed out that these " cloisons ", as he called them, extend down as far as the renal sinus in the middle third of the kidney and so divide the organ into compartments. " Cloisons " then—and now—is the word used by French anatomists to indicate an internal partition. Its obvious Latin equivalent is " septum ". Yet for some unknown reason the " Cloisons of Bertin " were referred to in subsequent anatomy books as " columnæ bertini ", and have so persisted. In further translation to the English language this error was preserved as the " columns of Bertin " (or Bertini, to make matters worse!). Whereas today, the structures are known simply as the " renal columns ".

This translation error has given rise to the idea that these cortical intrusions are in some way columnar in shape, whereas nothing could be further from the truth. They are, if freed of the medullary tissues they enclose, flangelike structures which intersect each other in a honeycomb fashion and so in fact " partition " the renal medulla into compartments, and the correct translation—" septa " of Bertin—could thus well be reintroduced into our anatomical textbooks, not only to do justice and right a 2-century wrong, but also to prefer a better definitive word.

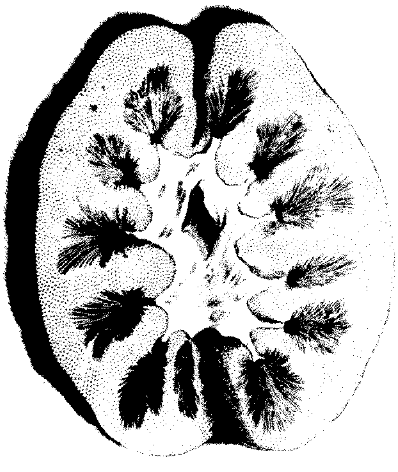

FIG. 1

One of Bertin's original illustrations showing the intrusions of glomerular (cortical) tissue which he termed " cloisons " (" septa ") extending right down to the renal sinus between the pyramids.

The Renal Lobes.—The " septa " of Bertin can more realistically be considered in a different light. In the conglomerate kidneys of the sea mammals, the ox and the bear, each renal lobe is separate from its neighbours and consists of a central mass of medullary tissue enveloped by a cortical layer on all sides except where the papilla emerges. The kidney in reality is thus made up of a group of small, separate, individual kidneys each with its separate

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blood supply and drainage (Fig. 2). Precisely the same pattern is found in the late human embryo, each lobe being distinct from, and indeed easily separated by gentle pressure from, its neighbour (Figs. 3, A and B). The grooves found on the surface of the kidney between the lobes at this stage correspond with the bases of the " septa of Bertin " and from them a thin layer of connective tissue passes deep into the renal substance between the 2 adjacent lobes. Each " septum " is thus divided into 2 halves by this layer of connective tissue, 1 half belonging to each of the 2 adjacent lobes. When the lobes are gently separated by pressure the plane of cleavage is down this connective tissue plane through the centre of each " septum " (Fig. 4).

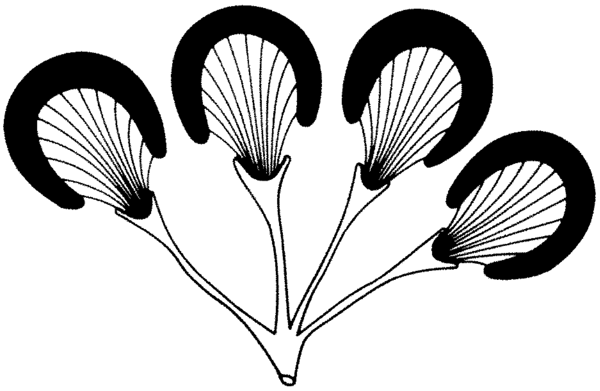
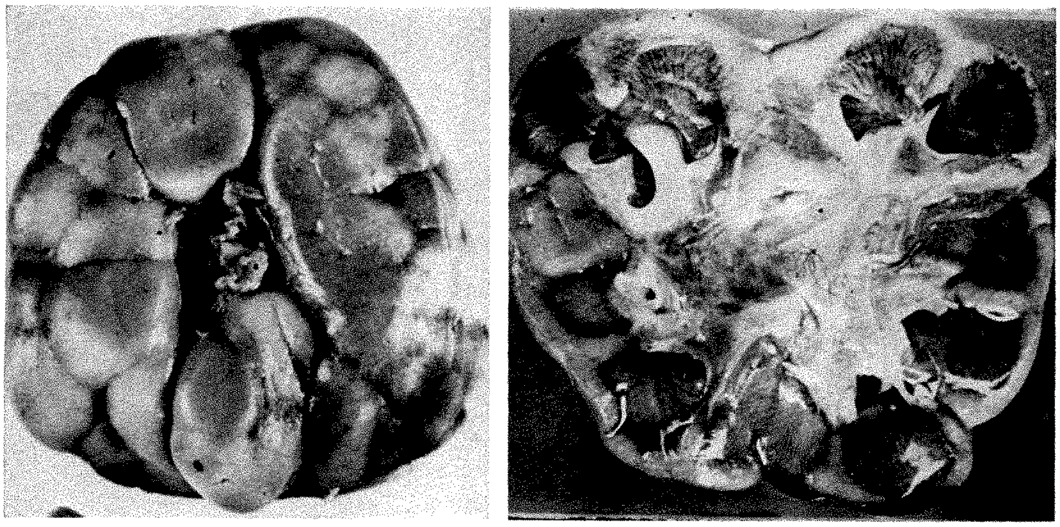


FIG. 2

Diagram of conglomerate kidney of sea mammals. The whole organ is the summation of multiple separate small " kidneys ", or renunculi, each of which has its own cortex and medulla and drains into a separate calyx.



A FIG. 3 B

A, Late human fœtal kidney: external surface showing well marked lobation, with deep grooves between the lobes. Gentle pressure easily separates the lobes along these planes of cleavage at this stage. B, Cut surface of 3, showing that the grooves between the lobes correspond to Bertin's " septa " enclosing medullary tissue.

As reference to the geometric concept of a renal lobe involves certain descriptive difficulties, for the sake of clarity the following scheme of nomenclature will be adopted throughout this paper. The lobe will be regarded as a central mass of medulla (the pyramid) surrounded on all sides, except where the papilla emerges, by a layer of cortex. The overall shape of this cortex will therefore be in the form of a deep-sided bowl.

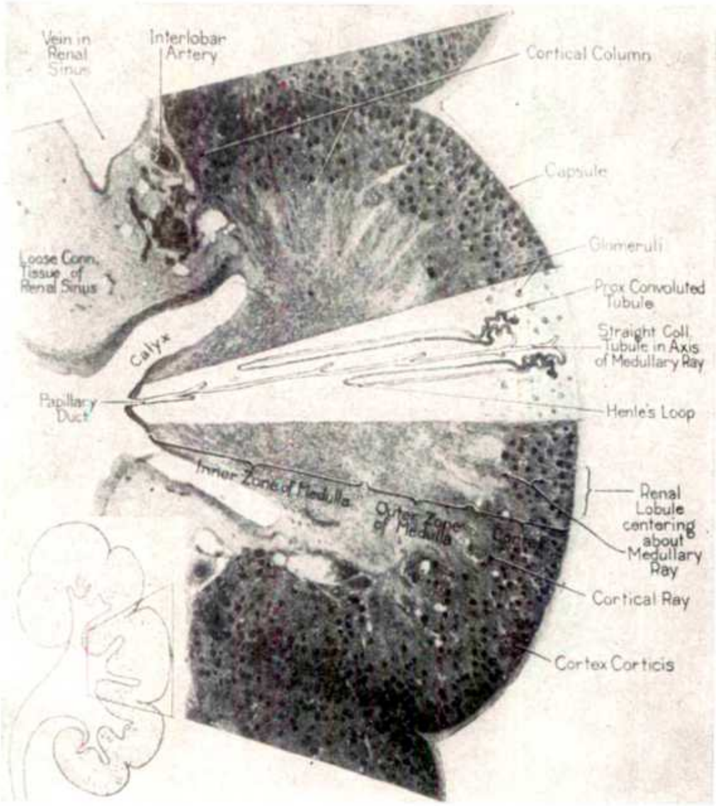


FIG. 4

Section of late human embryo kidney showing relationship of surface grooves, glomerular distribution and the " septa " of Bertin. The latter can be seen to be still divided near the surface into 2 separate lobar layers. At the inner edge of the " septa " are the interlobar vessels.

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As the lobes are arranged in the human kidney the side walls of each one is in contact with its neighbours. The cortical lobar " bowl " can usefully be divided into 2 parts; that which is in contact with the wall of an adjacent lobe, and that which has no such contact. The former is the wall of the bowl and will be referred to as the " septal " cortex; the latter forms the dome of the bowl and will be referred to as the " centrilobar " cortex.

The " septa " of Bertin are thus formed by the approximation of 2 layers of " septal " cortex of 2 adjacent lobes. In the adult these 2 layers are mainly fused (*i.e.* the late embryonic plane of cleavage is obliterated) and the grooves on the outer surface of the kidney become less distinct or disappear altogether (Fig. 5). The " septa ", as Bertin pointed out, reach as far as the renal sinus in the middle third of the kidney but are smaller and intrude less in the polar regions, where the lobes are generally less well defined. At times the septal cortex increases in thickness as it approaches the renal sinus and occasionally (as Bertin also indicated) forms a large mass or masses of glomerular tissue deep inside the kidney. These latter have on occasions been mistaken at arteriography for vascular tumours and nephrectomy performed. They have, therefore, somewhat dubiously earned the description of " cortical pseudo-tumours " in some radiological circles (Fig. 6).

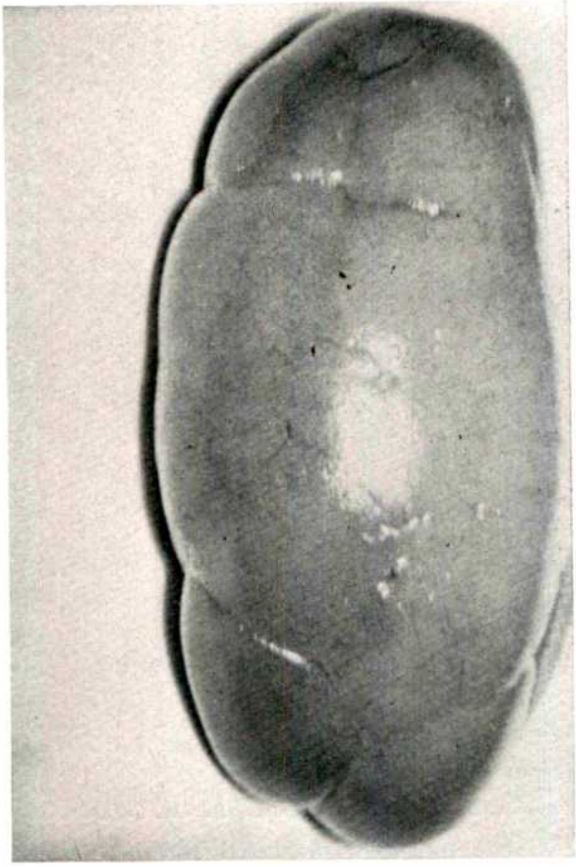


FIG. 5
Adult human kidney with capsule stripped showing faint interlobar grooves.

It thus follows that the glomeruli of one half of a " septum " drain into 1 papilla, whereas those on the opposite side of the " septum " drain into an adjacent papilla (Fig. 7).

It is logical, therefore, not to concentrate on the " septa " as single entities but to think in terms of lobes and regard them as made up of two layers of septal cortex (Fig. 8). The lobe is the major renal unit, a group of which in various stages of fusion, comprise the kidney. They have been named the " renunculi " in the past, to accentuate their claims as specific entities and have been thoroughly described by Löfgren (1949). They are somewhat comparable with the bronchopulmonary segments of the lung. Whereas the usual number of lobes in the human is 14 (Löfgren, 1949), this is obviously not a fundamental number, as many as 28 papillæ and calices may be encountered in some human kidneys and cross-sections of most kidneys show evidence of some further, though rudimentary, subdivision (Fig. 6). The actual number of NEONATAL papillæ present in any kidney probably represents the precise stage in the development of that kidney at which the onset of urine formation causes differentiation between calyx and collecting duct, as suggested by Osathanondh and Potter (1963).

Likewise the final ADULT number of papillæ and calices will depend on the degree of post-natal fusion and integration of renal lobes suggested by Sykes (1964). What factors lead to, or influence, this fusion are quite unknown, but the considerable morphological difference between neonatal and adult kidneys is apparently dependent on this process.

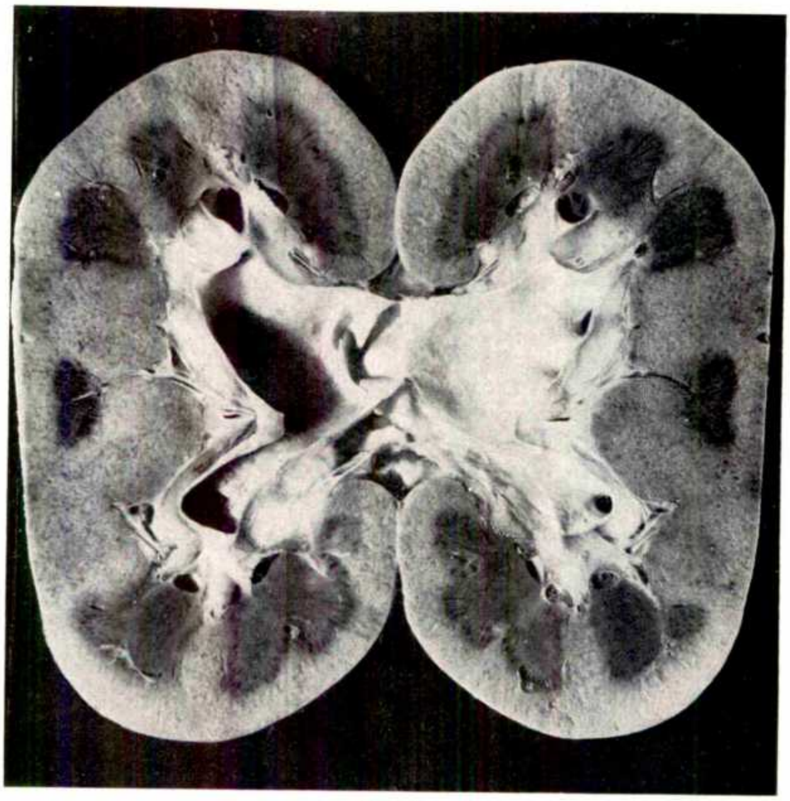


FIG. 6

Large " septa " forming deeply-situated masses of glomerular tissue in the mid-zone of a kidney in which there is a tendency to bifidity of the renal pelvis.

The Lobar Blood Supply.—The distribution of the major branches of the renal artery and its common variations have been described by various anatomists and more recently by Graves (1954), Boijsen (1959), Sykes (1964), and Fine and Keen (1966).

These vessels determine the major regions of supply and are important from a surgical point of view. As might be expected, however, the distribution of the more distal supply, interlobar and arcuate arteries, is governed by the lobar make-up of the individual kidney, and varies with the number of lobes. It also varies as to the number of arcuate branches given off per lobe from kidney to kidney, but much less between lobes in the same kidney.

There appears to be a basic plan governing the distribution of these middle-sized vessels, the result of which is the regular supply of arcuate vessels round each lobe and through them of a rather complex mass of cortical tissue throughout the kidney. The supply of the medulla is a secondary, post-glomerular event. This plan may then best be approached through a consideration of the distribution of the cortical tissue mass throughout the kidney.

The major portion of renal cortex is the subcapsular layer, 5 to 7 cm. deep, which extends under the entire surface of the kidney and which, from the lobar point of view, consists mainly of centrilobar cortex. At the hilus this layer folds inward and lines this entrance to the renal sinus.

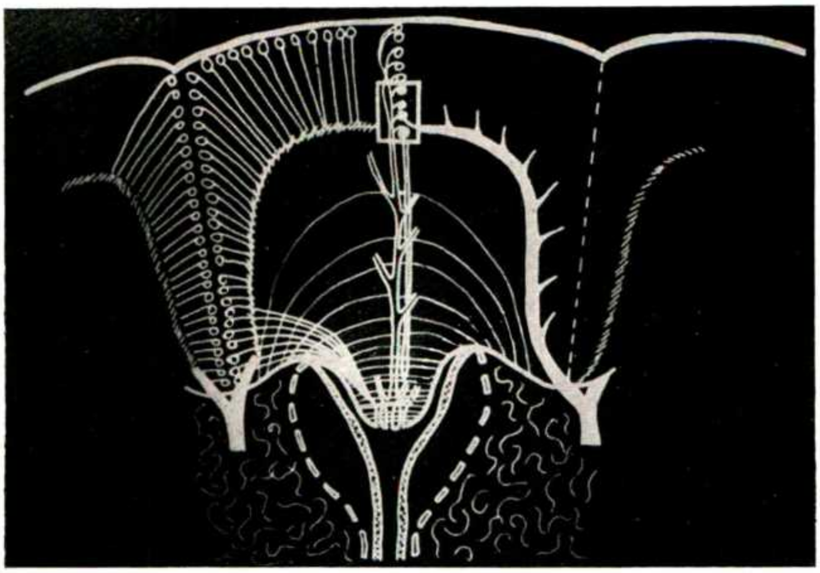


FIG. 7

Diagram similar to Fig. 4 showing (*a*) direction of nephron drainage from " septa " (only outer glomeruli of each lobe are indicated as far as medulla except in the inner part of one-half of a septum). Note " watershed " in central septum dividing lobes, (*b*) situation of arcuate arteries in cortico-medullary layer.

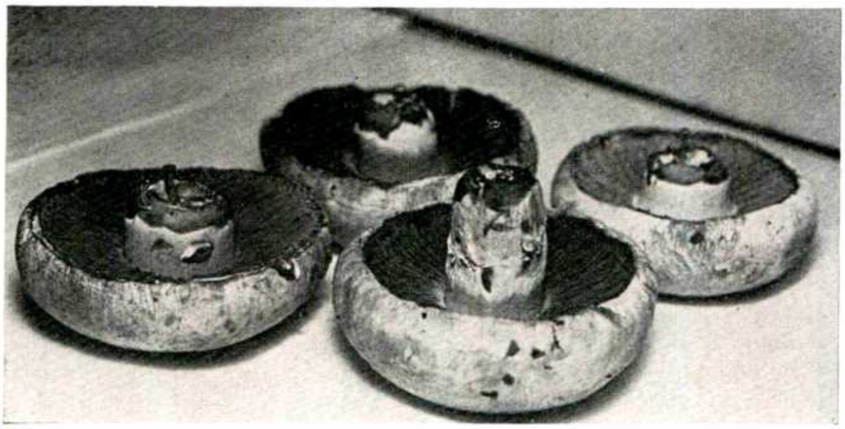


FIG. 8

Mushrooms fairly closely represent renal lobes in some respects and give a 3-dimensional idea of how the " septa " of Bertin are formed by fusion of cortical tissue from adjacent lobes.

In these folds—*the hilar lips*—the cortex is often thicker than elsewhere and might be considered as a special form of cortex. It consists, in fact, of the mural cortex of the relative lobes (Figs. 6, 15 and 16).

The " septa " of Bertin also consist of mural cortex and are deep ridges of cortical tissue extending between the pyramids and dividing the kidney up into compartments, the centre of which is occupied by the pyramids. On the opposite side of the kidney to the hilus, a large, somewhat zig-zag, *longitudinal* " *septum* " extends from pole to pole between the anterior and posterior groups of papillæ, commonly reaching down to or even projecting into the renal sinus (Figs. 14 and 15). Connecting this single longitudinal " septum " to the " hilar lips " in the mid-zone of the kidney are *transverse* "*septa* " which pass between the papillæ and, again, often project into the renal sinus as blunt ridges. In the polar regions these " septa " are typically much smaller, do not reach down to the renal sinus and spread in a vaguely radial pattern from the " hilar lips ".

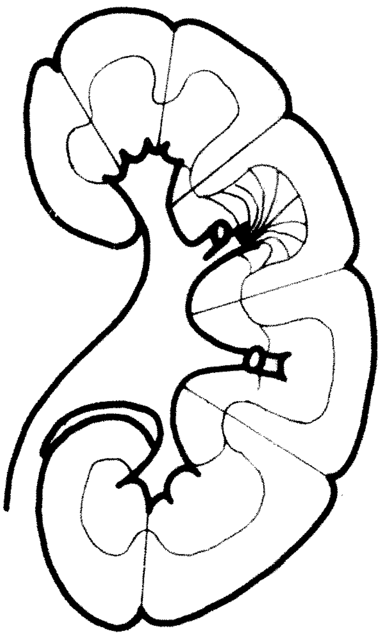


FIG. 9

Diagram showing relationship of " septa " of Bertin and the anterior renal lobes in adult kidneys.

These 3 groups of cortex, subcapsular, hilar lips and " septa " of Bertin require to be supplied by arcuate vessels at frequent intervals. This is achieved as follows. As the main branches of the renal artery pass through the hilus they divide, if they have not already done so, into branches some of which are destined for the polar regions and some for the mid-zone lobes. The former often do not branch further until well into the renal sinus. The latter, but also occasionally the former, usually give off their first arcuate branches to supply the cortex of the hilar lips before they have reached the renal sinus proper (Figs. 10, B and 13). At this point they usually lie on the junction between the transverse " septa " and " hilar lips " and from then on simply run on along the ridges of the transverse septa lying in the fat of the renal sinus and giving off paired arcuate branches to the lobes on either side (Figs. 10 and 13). The latter also traverse the fat of the renal sinus for a few millimeters before entering the renal substance proper at the junction between the cortex of the " septum " and the medulla of the pyramid. The unembedded length of the arcuate vessels will depend on how far the septal ridges project into the sinus beyond the medullary tissue.

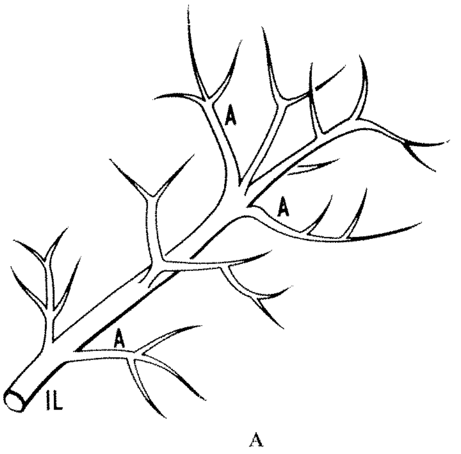
When the interlobar vessels later reach the junction between the traverse " septum " on which they lie and the " longitudinal septum " they divide into their terminal spray of from 4 to 6 vessels (arcuate) which fan out over the cortex of the junction to supply the outer portions of the lobes, again entering the renal substance at the cortico-medullary junction. It is from these arcuates that the longitudinal " septum " usually derives its blood supply (Figs. 10, 11, 13, 14, 19).

Occasionally, however, a large vessel is found to run along the inner edge of the " longitudinal septum " giving off branches to the adjacent portions of both anterior and posterior lobes. This artery which is a true " interpapillary artery " has been described in detail by Fine and Keen (1966) and Engelbrecht *et al.* (1969).

Arcuate vessels in general enter the kidney substance at the cortico-medullary junction between the " septa " and papillæ shortly after their origin and traverse it still in the plane of the *cortico-medullary junction* of each lobe, giving off the small interlobular vessels from their outer aspects and with little supply passing centrally to the medulla other than the occasional arteriole recta spuria. They terminate about half-way across the " dome " of the lobe, closely resembling the fanning ribs supporting the dome of a Gothic building. Each supplies either an eighth or tenth or less of the total cortex of the lobe and there is little or no anastamosis between these supplies (Figs. 7, 10, 11, 12 and 13).

Considered from the lobar point of view this pattern of distribution means that each lobe derives its blood supply from 2 or 3 but rarely more separate *interlobar* vessels (Figs. 10, 11 and 13).

With regard to nomenclature there is some confusion relating to " segmental " vessels, this term having been applied variously to the main branches of the renal artery and to interlobar vessels as they traverse the renal sinus. It seems logical to take the view that as soon as a vessel gives rise to an arcuate artery it becomes an interlobar artery. If this is accepted the majority of vessels that enter the hilus almost immediately become interlobar vessels as their first arcuate branches are to the cortical tissue forming the lips of the hilus. The term " segmental vessel " should therefore be confined to branches before they give off their first arcuate. An occasional vessel traverses the renal sinus to its outer limit before breaking up into terminal arcuates. Such vessels do not travel along the inner edges of the " septa " and are often situated in the polar regions; there is no particular reason why these should be singled out as " segmental " vessels apart from this peculiarity.



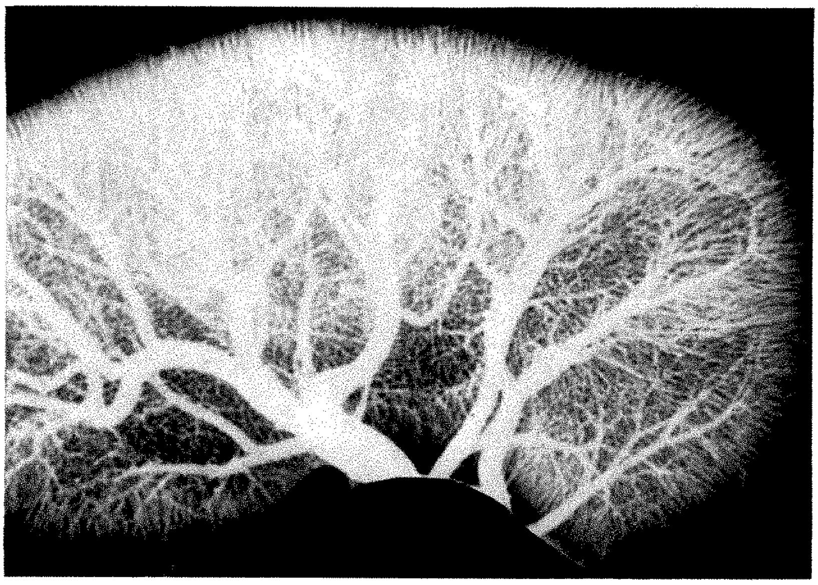
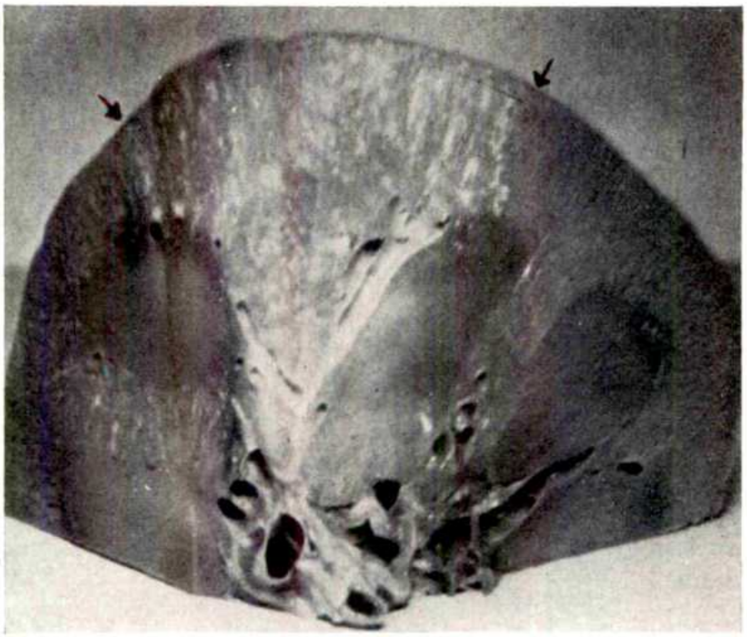
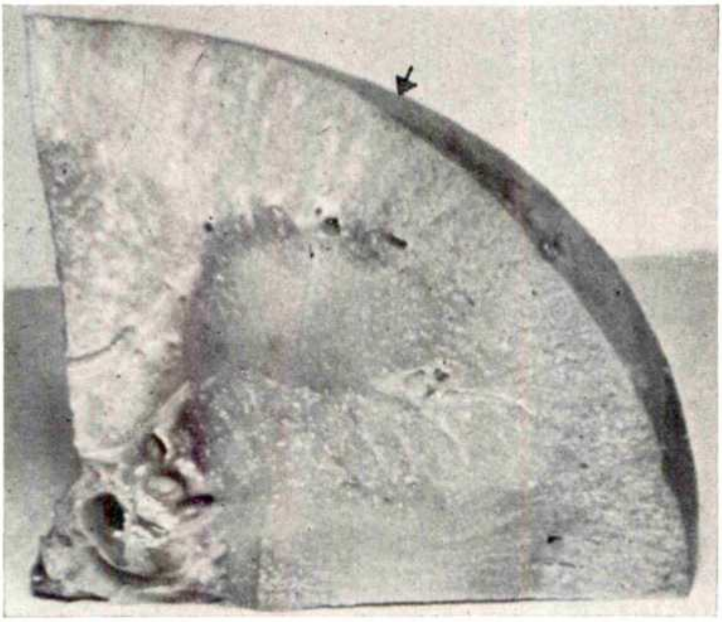


FIG. 10
A, Diagram showing typical pattern of branching of arcuate vessels from the interlobar vessel (usually 5 to 7 lateral branches). B, Radiograph of injected human kidney showing interlobar and arcuate branching in relationship to " septa " and the arcuate supply to the renal lobes.



A



B

FIG. 11

A, Wedge of human kidney with interlobar vessel injected with "chromopaque" and sectioned at right angles through adjacent lobes. The relevant arcuate supply is shown to extend only half-way across the glomerular zone of the 2 adjacent renal lobes. (Indicated by arrows.) B, Another view showing extent of individual arcuate supply extending only half-way across a renal lobe.

The " Offsetting " of the Lobar Pattern.—If, in its horizontal cross-section, the renal hilus opened on to the exact medial border of the kidney the anterior and posterior groups of lobes might be expected to be mirror images of each other, arranged symmetrically to the coronal plane of the kidney and with the " septa " between them running directly along the antihilar (lateral) border of the kidney.

Fig. 12.—Diagram of section showing extent of arcuate supplies to adjacent lobes from an interlobar artery.

Fig. 13.—A, Diagram showing the distribution of the arcuate supplies to cortex. A = first arcuates to " hilar lips ". B = lateral arcuates to mural cortex. C = polar interlobar vessel without lateral arcuates. D = terminal spray of arcuates. B, Same supply related to cortex (white) and medullar (hatched). Note the interlobar vessels lying on transverse " septa " and the lateral arcuates entering tissue at cortico-medullary junction. Each mid-zone lobe is supplied by 8 to 10 arcuates at intervals round its circumference.

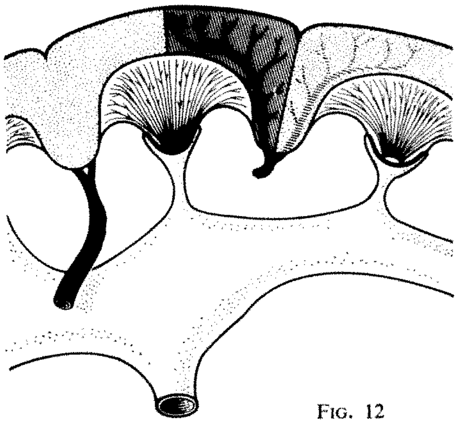
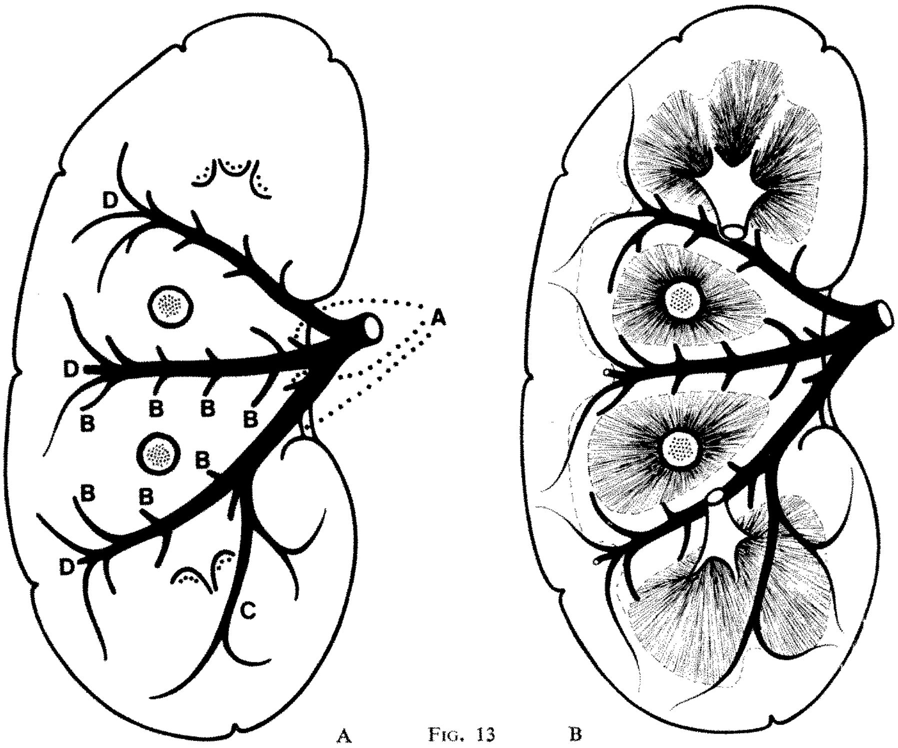


FIG. 12



A FIG. 13 B

In the majority of kidneys, however, the hilus opens on to the anterior surface of the kidney, near its medial border, and as a result the two groups of lobes are offset relative to the main renal coronal plane, the longitudinal " septum " between them lying on the posterior surface of the kidney, near its lateral border. A further result of this offsetting is that the anterior papillæ lie laterally, and the posterior papillæ posteriorly and more medially, relative to one another (Figs. 14, 15 and 16). In the less common instances in which the hilus opens on to the posterior aspect of the kidney this arrangement is reversed.

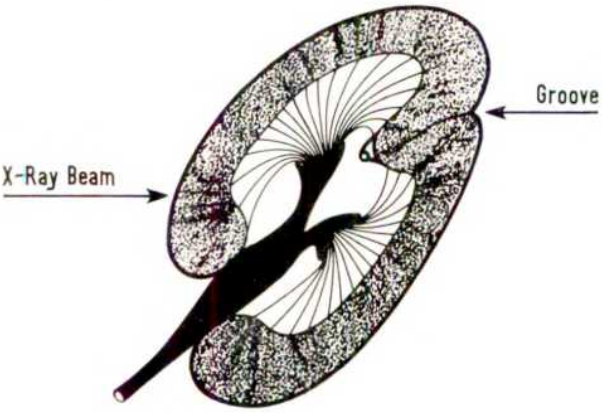


FIG. 14

Diagram of cross-section of the mid-zone of a human kidney showing " offsetting " of renal lobes. The hilus opens on to the anterior surface and the longitudinal " antihilar " or " interpapillary " " septum " lies roughly opposite it on the posterior surface (smaller arrow). The large arrow shows the direction of the AP X-ray beam in the supine position. The anterior papillae are projected in profile and lie lateral to the posterior ones, which appear " end-on " in the radiograph.

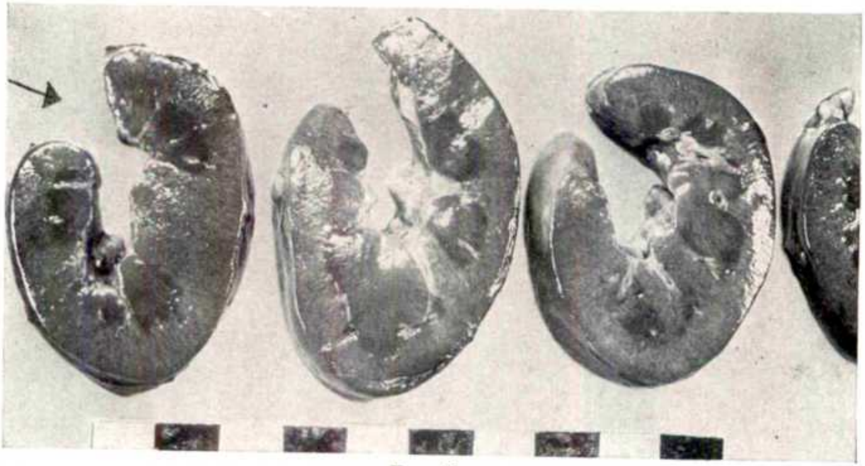


FIG. 15

Actual cross-sections of human kidney showing " offsetting " of lobes, and the positions of the anterior and posterior mid-zone papillæ.

The Polar Regions.—In the two polar regions considerably more fusion of lobes occurs than in the mid-zone. This has two main results, (*a*) as mentioned before, the " septa " of Bertin are less well developed, do not completely separate off the lobes and may project little more than a few millimetres inwards from the centrilobar cortex, (*b*) The pyramids and papillæ are also fused in varying degrees and, as there is usually only 1 calycine stem draining each pole, the result is the well-known variety of compound papillæ and conjoined calyces which drain these fused polar lobes. As well, the renal substance thickness is normally always greater in the polar than in the mid-zone regions; a point of importance in the early recognition of the large polar scars of atrophic pyelonephritis in children.

APPLICATIONS

The concept of a lobar structure in the kidney affects many clinical and pathological practical matters and theoretical points of view. A few examples may be given.

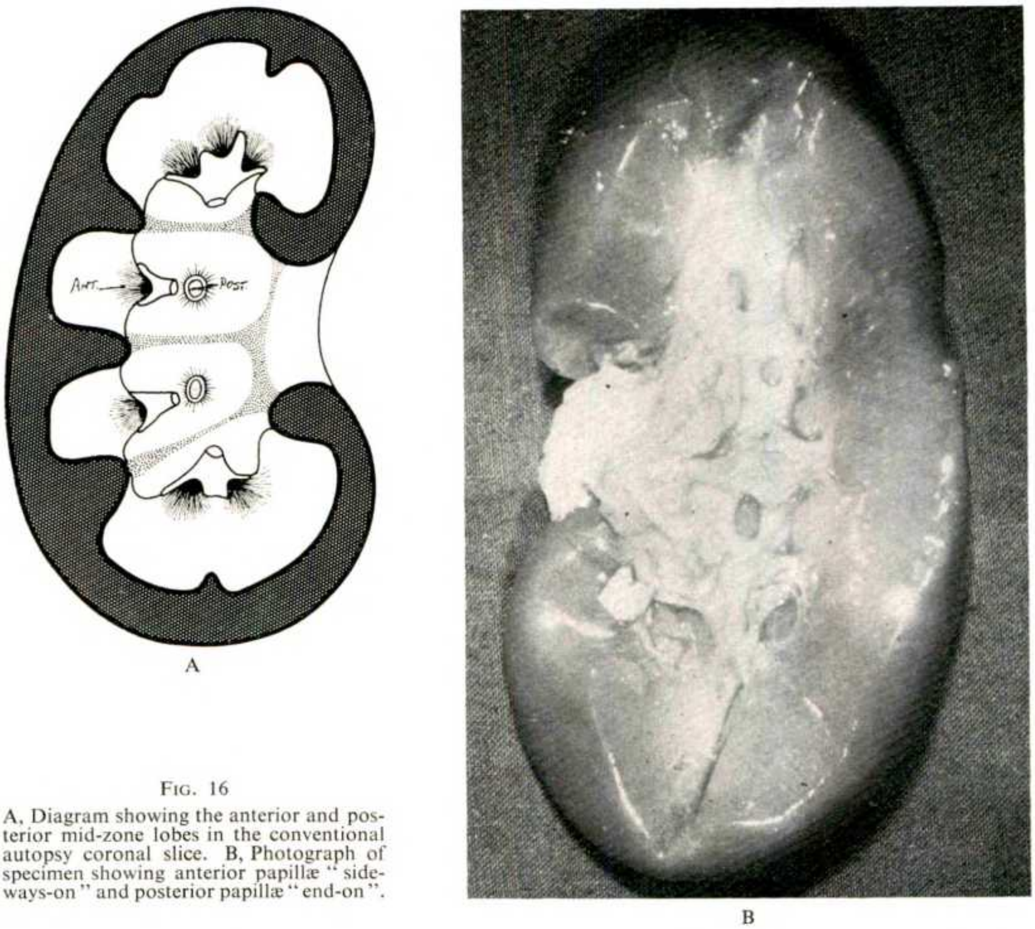


FIG. 16

A, Diagram showing the anterior and posterior mid-zone lobes in the conventional autopsy coronal slice. B, Photograph of specimen showing anterior papillæ " sideways-on " and posterior papillæ " end-on ".

1. *The " offsetting " of the Lobes*.—Two practical points arise from this distribution. In the autopsy room a common method of examining the kidney is by a single cut, roughly through its mid-coronal plane. This usually slices through the anterior lobes and papillæ in a plane which is very near to their true mid-lobar section and they are well displayed as a result. The posterior lobes and papillæ, on the other hand, are not touched (Figs. 14, 15 and 16). The second point, a valuable one, is that the conventional anterioposterior supine view of the abdomen obtained during urography also gives an almost true mid-sectional representation of the anterior lobes, and so allows an accurate measurement of the thickness of the renal substance from papillary tip to the surface. Any condition causing a diffuse increase or decrease in the mass of renal parenchyma affects this measurement and this, together with the overall length of the kidney, is as accurate a means of assessing renal mass by indirect methods (radiography) as we possess (Figs. 15 and 16).

The anterior papillæ are those seen to lie outermost in the urogram in the majority of cases. The posterior papillæ are seen more medially and " end on ". Accurate localisation of a stone is thus possible in a single-plane radiograph in kidneys where this " offsetting " is well established.

2. *Obstructive Atrophy.*—In serial studies of the morphological changes resulting from complete ureteric obstruction in the pig (a multi-papillary kidney very similar in many respects to that of man), Matz (1969) showed that a greatly increased tempo of changes occurred in the fourth week. This change was located maximally in those nephrons draining the deep (parasinous) parts of the septal cortex and the explanation was that it was due to 2 factors, (*a*) the direct force of the dilating calicine fornix acting at right angles to the general direction of flow of the nephron structures and collecting tubes in this region, and (*b*) the compressive force of 2 adjacent dilating calices squeezing the inner part of the intervening " septum ", the more central part of the lobe being unaffected by these local factors (Fig. 17).

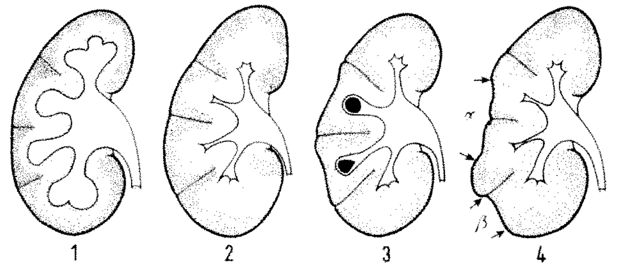


FIG. 17

Differentiation of focal disease by lobar alterations.

1. *Obstructive Atrophy*

Generalised narrowing of renal substance; generalised recession of papillæ of equal degree throughout kidney; generalised narrowing of glomerular zone more marked in " septa " which are pinched between ballooned calices; smooth renal outline. (Differentiation between glomerular zone and medulla often unsharp.)

2. *Normal*

3. *Papillary necrosis* (with two papillæ separated)

Surface depressions in centrilobar area with associated narrowing of glomerular zone. This may extend down one-half of a " septum " of Bertin or may be limited to the centrilobar area in which case the " septa " may be hypertrophied (Kincaid-Smith), or one-half of a " septum " may be narrowed and the other hypertrophied depending on the distribution of the necrotic zone. The renal outline is indented.

4. *Ischaemia* (partial infarction)

Alpha: in distribution of interlobar artery; Surface depression centred on interlobar groove; focal narrowing of glomerular zone extending half-way across adjacent lobes and involving whole of intervening " septum ". Beta: in distribution of arcuate artery; same as in alpha but only involving a sector of 1 lobe and its half of a " septum ", and a sector of its papilla. Renal outline indented.

3. *In Chronic Obstructive Atrophy* the organic changes in the experimental animal decrease in degree from within outwards relative to the renal lobe. After short periods of obstruction followed by a suitable repair period, the inner nephrons (those in or near the cortico-medullary junction) are the first to show tubular degeneration, as their long loops of Henle reach well down towards the papillary tip. For a while their glomeruli survive without any tubular connection and later they, too, disappear leaving very little trace behind. The outer (sub-capsular) layers of nephrons, with their much shorter loops of Henle, are less affected and survive (Fig. 4).

As so little trace is left of the previously damaged nephron population, it seems likely that at present many examples of minor degrees of obstructive atrophy are missed by the histologist, the residual histological changes being non-specific. It appears that the only way of detecting that this damage has occurred previously would be by counting what might be termed the " layers " of glomeruli lying between medulla and capsule. The average number of these " layers " in the human adult kidney appears to be between 10 and 14. A diminution in their number without arteriosclerosis would be indicative of some such generalised nephron loss.

Such a count must, of course, be made in a true mid-lobar cross-section to obtain a reliable result. Indeed any assessment of true cortical thickness must be carried out in the true mid-cross-section of a lobe. The usual single autopsy section is fortuitously near this plane with regard to the anterior lobes of many, but not all, kidneys. The author's experience is that multiple cross-sections appear to be the simplest way of examining the kidney from a lobar point of view (Fig. 15).

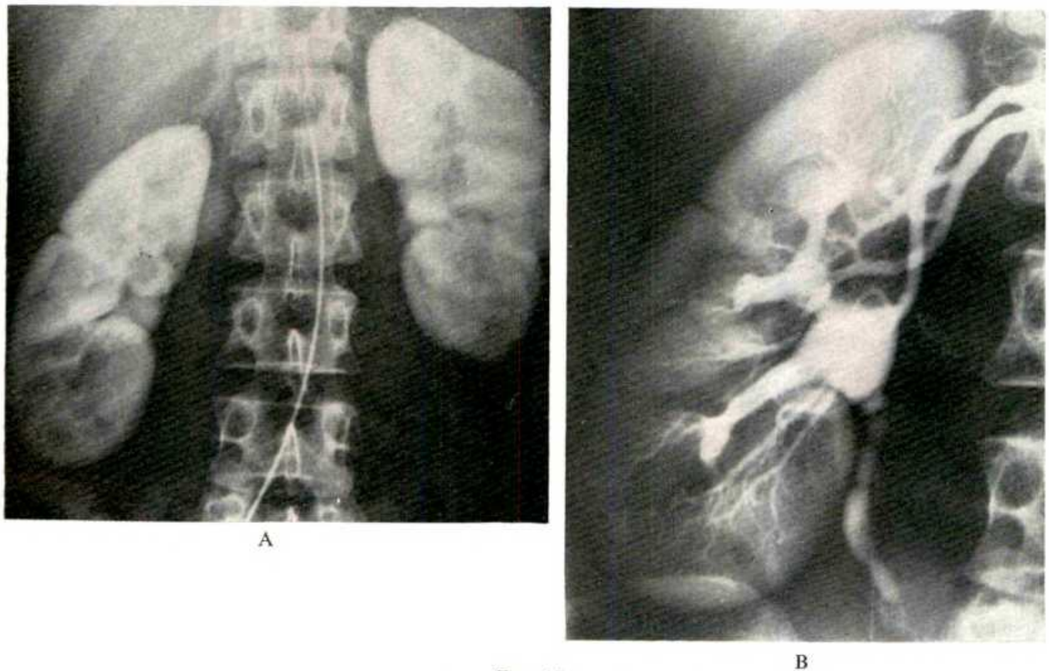


FIG. 18
Persistant fœtal lobation.

A, Nephrogram phase or a pair of human kidneys showing well defined lobation; the relationship of the surface grooves to the " septa " is particularly well shown. B, Second injection showing combined arteriography and urography. The relationships of interlobar arteries " septa " and calyces is well demonstrated.

4. In *papillary necrosis* due to prolonged analgesic ingestion, Kincaid-Smith (1967) has pointed out that there is often hypertrophy of the " septal ' and atrophy of the " central lobar " cortex in a lobe. In advanced cases, where the whole papilla is destroyed, the atrophy may be seen to extend throughout the whole glomerular tissue of the lobe, including the septal cortex (Figs. 3 and 17). It seems that a logical explanation for the distribution of atrophy and hypertrophy in the early cases is that the necrotic area is still confined to the central part of the papilla and interrupts and obstructs only those nephrons traversing it. The remainder of the nephrons of the lobe, namely those arising in the " septal cortex " would still have free drainage and might be expected to hypertrophy (Fig. 17).

5. The large amounts of glomerular tissue (septal cortex) lying deep within the kidney substance react in a similar manner to the centrilobar cortex in conditions which primarily effect the smaller vessels and glomeruli. For example, the extensive generalised diminution in thickness of cortex which occurs in long-standing *peripheral arterial disease* (and chronic glomerular nephritis) results in marked reduction in the size and depth of the " septa " of Bertin. This is

partly compensated for by loss in overall kidney bulk and partly by an increase in sinus fat (" Lipomatosis ").

6. *Embolism or thrombosis* of a branch of the renal artery will result in infarction over an area which will depend on the size of the vessel involved.

If only an *arcuate vessel* is affected the area of damage will be confined only to its territory of supply, comprising a sector of one lobe not larger than an eighth of the total lobe, which will include both septal cortex (1 side of a " septum " only) and a similar sector of papilla. An *interlobar artery* thrombosis, however, will involve adjacent sectors of 2, or even 3, lobes and the whole width of the " septum " between them, but not the whole of any 1 lobe or any 1 papilla. This may account for the preservation of the renal papilla in infarct scars described by Smith (1962). At least two adjacent interlobar vessels would require to be involved for a whole lobe or papilla to be affected (Figs. 4, 7, 11, 12 and 17).

In this context it is perhaps worth noting that the part of a lobe furthest from the main vessels is a point somewhere near the middle of its dome, at the confluence of the arcuate arterial segments.

7. To the *surgeon* the lobar anatomy is as valuable as the concept of bronchopulmonary segments in the lung from the point of view of locating disease, *e.g.* a stone. But, unlike the bronchopulmonary segments, is less helpful from the point of view of localised resection of tissue, because the blood supply is on a non-lobar basis. To resect a lobe, or to perform a partial nephrectomy on a lobar basis, the incision would have to be along the mid-plane of the " septa " of Bertin surrounding the part to be resected, with ligation of the arcuate arteries rising from that side of the relative interlobar vessel. This would ensure leaving behind a minimal amount of ischæmic tissue but is hardly a practicable procedure. It also follows that an incision through the grooves of a " septum " of Bertin will involve only interlobular vessels until the arcuate and interlobar vessels lying on its inner edge are reached; with the exception, in some kidneys, of the longitudinal interpapillary " septum ". *i.e.* the " bloodless plane of Brodel ".

8. From the point of view of *renal biopsy* the posterior surface of the lower pole is the part usually entered. Here there is a fair chance of obtaining both cortex and medulla from a deep punch. On the other hand if a " septum " only is traversed by the needle a sample containing only renal cortex may be obtained right down to the renal sinus. Thirdly cortex, medulla and again " cortex " may be sampled by the needle entering a deeply-situated " septum ".

9. *From the radiological point of view* the lobar structure has several points of interest. It rationalises the calycine distribution and provides a relationship between it and the pattern of vascularity in the arterial and capillary phases of arteriography and tomography. Using the former, the interlobar vessels can be seen to be distributed between the calices at regular intervals and the arcuate vessels may usually be defined. Any slight disturbance of this pattern, *i.e.* the loss of an interlobar vessel from infarction, or its displacement by an early tumour, is readily detected. Extra vessels supplying malignant tumours can be sorted out and correct identity of " pseudo tumours " of glomerular tissue identified (Figs. 6 and 18).

" *Fœtal lobation* " is seen to correspond with the distribution of the anterior calyces, the surface notches lying between calyces, and the localised hypertrophy of surviving lobes in advanced pyelonephritis to be associated with surviving papillæ. The difference in appearance between advanced papillary necrosis and pyelonephritic scarring may also be explicable on this basis (to be published at a later date).

Other features of kidney disease may well be related to the lobar structure. Certain methods of measurement, particularly isotopic autoscans, must take it into account. The concept is certainly an advance on the generally held idea that the human kidney resembles the unipapillary kidney of many laboratory animals.

My thanks are due to the Curator of the Museum of the Royal College of Surgeons (England) for his kind permission to publish Fig. 6; to Dr R. G. Bernstein of New York for sending me the radiographs of Fig. 18; to Dr Merlin of the Royal Veterinary College, London, who was unconsciously responsible for rousing my interest in the comparative anatomy of the kidney, and to many friends who have shown an interest in this concept, and suggested its publication.

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CRACKING OF VESICAL CALCULI BY CAPACITOR DISCHARGE

By D. M. WALLACE, P. F. COLE and K. L. DAVIES

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VESICAL stones whether small or large are conventionally removed by either open or closed methods. The open method may be associated with other surgical procedures, but in any case, involves hospitalisation of approximately 2 weeks. The closed method, using the blind lithotrite or the visual cystoscopic lithotrite necessitates grasping the stone firmly between the jaws of the lithotrite and then applying compression. With the visual lithotrite there is a limit to the size of the stone that can be grasped and even with the classical non-visual lithotrite there is a limiting size of stone that can be grasped conveniently. The tensile strength of the lithotrite blades also limits the size of stone that can be crushed without risk of fracturing the lithotrite blades.

In this new technique with an instrument known as the electronic lithoclast, vesical calculi are broken up by a series of nearby powerful electrical discharges. Important advantages over other methods lie with the ease of bringing the high voltage electrode into immediate contact with the vesical stone and the elimination of difficulties encountered in gripping a stone in the jaws of a lithotrite.

In designing a cystoscopic instrument certain facts were considered.

1. Because of the turbidity of the medium after discharge, a good irrigating system of the order of 500 ml. per minute was considered to be essential.

2. Since it was essential that the spark gap unit be placed in contact visually as well as by palpation, the best possible optical system was mandatory. The telescope fitted to the modified Riches Kidd diathermy cystoscope has a better field than any other comparable cystoscope and was therefore used.

3. It was felt that here was a cardinal indication for fibre-optic light illumination since the shock sensitive lamp filament of the conventional cystoscope would be liable to break if subjected to the shock wave in the neighbourhood of the stone.

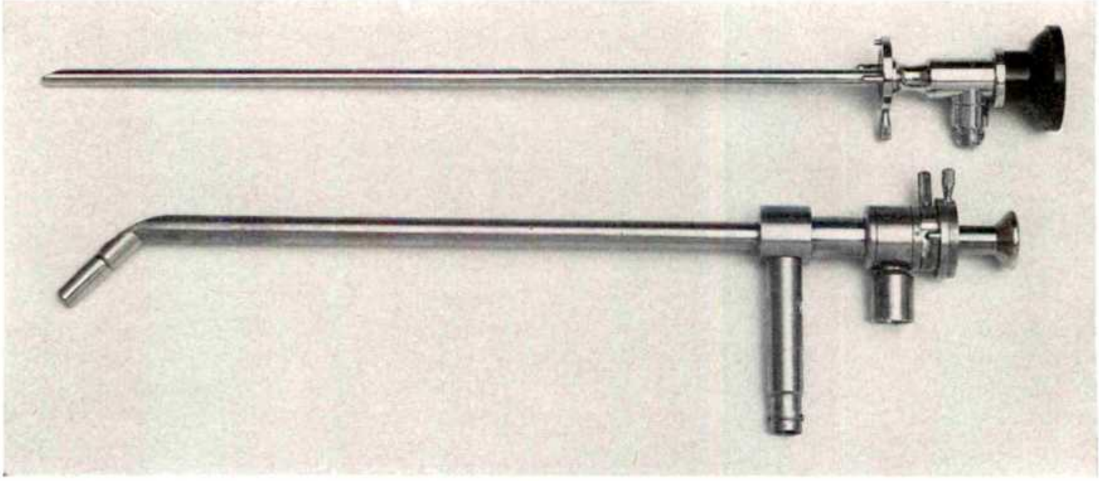


FIG. 1

Cystoscope and Fibre Lit for oblique angle telescope.

Principles of Operation.—The underlying principle of the method is that all types of bladder stones, although hard and compact, have an amorphous structure which makes them particularly vulnerable to shock damage. If a shock wave is generated by means of a high voltage discharge and the energy focused directly on to the stone surface, the stone can be broken up with comparative ease. Almost invariably the effect of such a discharge is to shatter the stone into a large number of variable sized fragments, many of which are small enough to be washed out through the irrigation channel of a standard cystoscope. The larger remaining fragments are shattered with a second or possibly a third additional discharge. With a large stone, it is found in general, that between 10 and 20 discharges are required to achieve complete disintegration.

With the device, the electrical discharge takes place between a central electrode and a brass ferrule in contact with a sheath of the cystoscope which acts as part of the earth return. Firing occurs when a previously charged, low inductance, high voltage capacitor is discharged by triggering a spark gap placed in series with it, as shown in the circuit below.

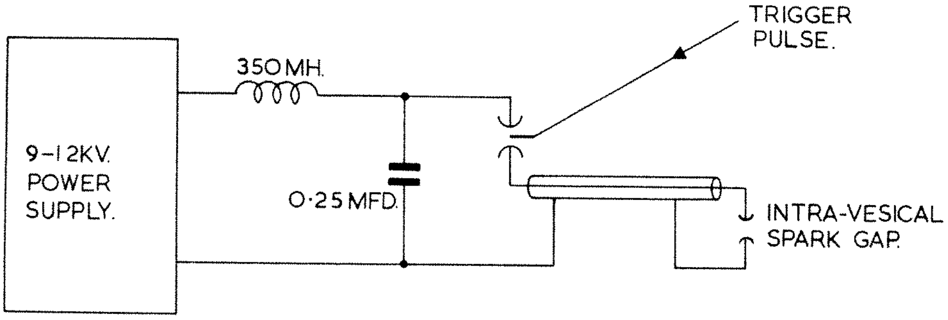


FIG. 2
Circuit diagram of Lithoclast System.

Technical Description of the Unit.—The electrical discharge at the intravesical spark gap is produced by the discharge of a low inductance 0·25/μF 12 kV capacitor. Switching is achieved by means of a 3-electrode trigger spark gap within the unit, activated by a trigger signal from a pulse transformer fed in turn by discharging a capacitor with a silicon controlled rectifier. The high voltage capacitor charging circuit consists of a 28 V rechargeable nickel cadmium battery feeding a converter and voltage multiplier and suitably arranged with a feed back loop through an energy range switch and amplifier to limit the charging voltage. There are 4 pre-set energy ranges corresponding to charging voltages of 9, 10, 11 and 12 kV which in turn give output energies of 10, 12·5, 15 and 18 joules respectively. As a result of the early clinical trials parallel charge and trigger controls have been incorporated in a footswitch for ease of operation. An audio signal has been provided to indicate when the unit is ready for firing, and the unit can also be operated directly from the mains supply.

The present " EHT Ready " lamp is fed by a separate circuit which monitors the voltage on the capacitor. For this a unijunction transistor is employed whose b.2 voltage is set by the energy range switch. This unijunction triggers approximately 300 volts below the stabilised charging voltage and feeds a silicon controlled rectifier which causes the EHT lamp to glow. The battery charging circuit is voltage and current limited and, with a very low battery, it reaches a maximum of about 50 mA; as the battery charges, the current falls and the fully charged battery is finally fed with less than 10 mA. In normal use, a fully charged battery should last for at least 200 firings before needing a recharge. The minimum interval to be allowed between successive firings is approximately ten seconds.

Pre-Clinical Experiments.—Before attempting to use the lithoclast clinically, it was first subjected to extensive trials *in vitro*. Initially, attempts were made to see if there was danger of

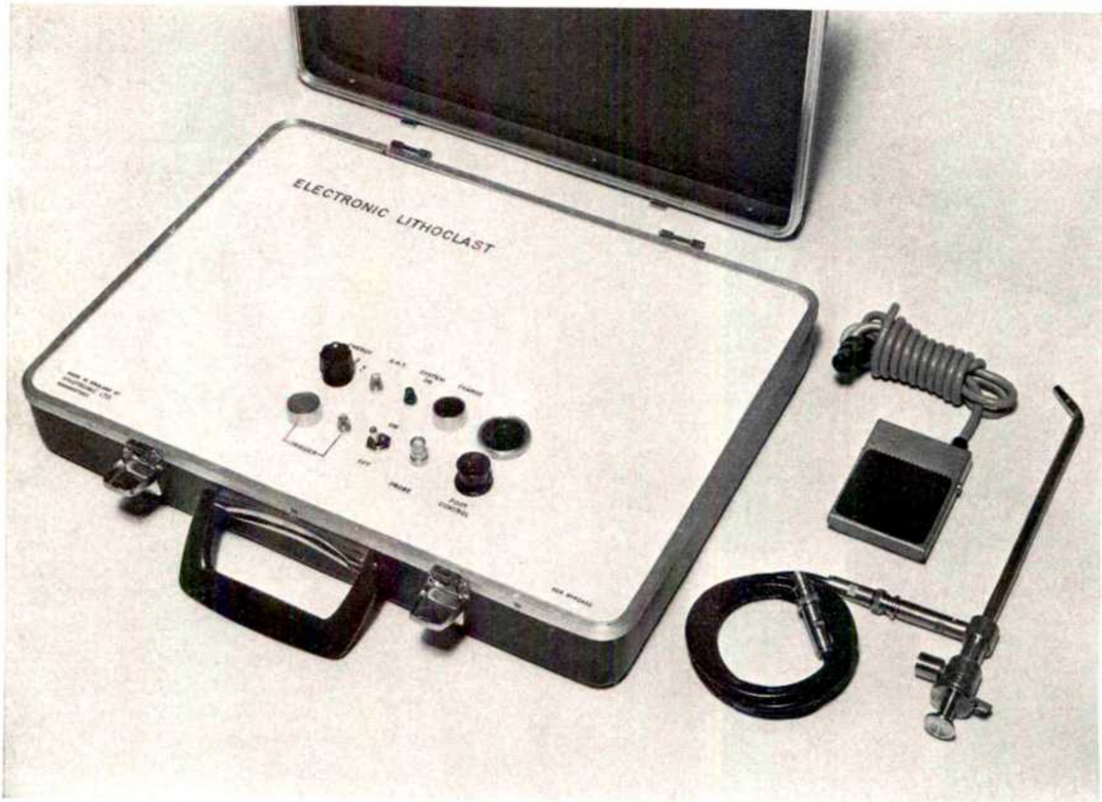


FIG. 3
Electronic Lithoclast charging unit, footswitch and cytoscope.

patients receiving electric shocks and to test this the HV capacitor was discharged across the spark gap immersed in water, held in a volunteer's cupped hands and positioned about $\frac{3}{4}$ inch from the skin. Discharges were noisy and spectacular but no electric shocks were obtained. A violent physical force is, however, experienced similar to the sensation of catching a cricket ball.

Following this preliminary test, a prototype unit was tested with various types of specimen bladder stones. These were placed in a plastic beaker of water and the spark gap positioned in contact with the stones and at various distances away. In contact and at distances up to 2 to 3 mm., the stones were shattered very successfully while at 5 mm. and beyond, discharges had little or no effect. Tests with the cystoscopic telescope likewise proved very satisfactory, although after each firing, the water became intensely cloudy and even with fibre-optic illumination, it was often difficult to find many of the resulting fragments. However, waiting a few minutes for the debris to settle or changing the water solved this problem.

During these tests, the main problem that came to light was the design and construction of the vesical spark gap. From the point of view of withstanding physical damage from the discharge, experiments showed that P.T.F.E. was a better insulator than either polythene, nylon or fibreglass and general use of this was therefore adopted. It was also found necessary to prevent the high voltage electrode being forced down into the insulator by the discharges. So as not to complicate the spark gap replacement procedure, this was found to be best achieved by using a small cone of P.T.F.E., and a small brass bush so positioned that the action of screwing home the brass ferrule into the sheath squeezed the P.T.F.E. cone against the H.V. cable and clamped it into the fixed position. The following diagram shows this in greater detail. It should be mentioned that the leading edge is streamlined as much as possible to facilitate passage through the urethra.

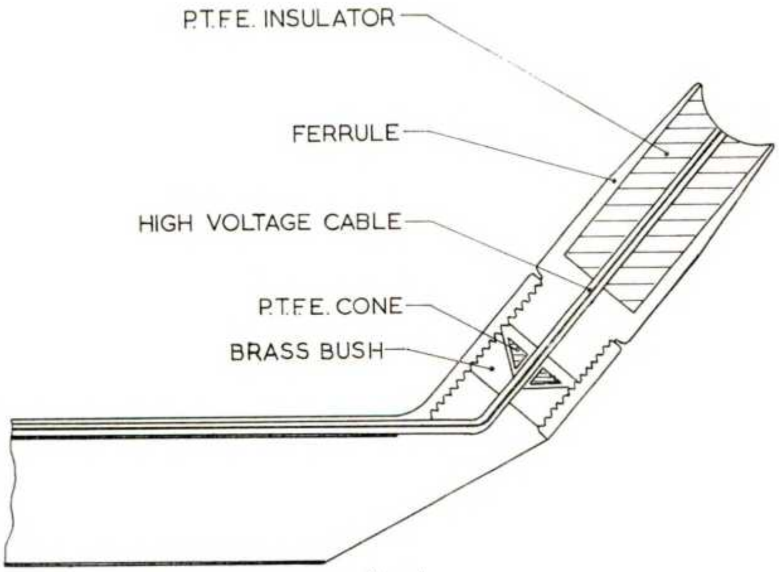


FIG. 4
Cross-sectional view of Intra-vesical Spark Gap

Clinical Trials.—The first clinical tests with the electronic lithoclast were performed on an elderly male patient whose bladder was opened surgically and contained multiple stones. The bladder was filled with water and the lithoclast used exactly as when the stones were placed in a plastic beaker. The bladder wall remained free of damage and although the discharges caused the E.C.G. chart recorder trace momentarily to go off scale, this effect was due to electronic interference and no alteration in cardiac activity was observed.

The second trial involved a male subject aged 70 with a large calcium phosphate bladder stone. He was placed under general anæsthetic and the lithoclast probe inserted directly into the bladder with the urethra dilated to 26-28 (F). Approximately 15 discharges which were audible to the by-stander (and both audible and internally visible to the surgeon) were required to shatter the stone into small particles; these were periodically removed by bladder irrigations. No difficulties or side-effects were experienced by the surgeon during the short operation and once again no damage to the bladder wall was observed. Slight muscular spasms occurred during several of the discharges, but these had no observable effect on the heart monitor oscilloscope screen. The patient was subsequently discharged from hospital 3 days later.

As far as the unit itself was concerned, subsequent examination of the vesical spark gap showed that although the P.T.F.E. insulator was still sound, the leading edge of the surrounding tapered brass ferrule was considerably eroded and quite sharp in places. On account of this damage, it is recommended that the vesical spark unit should not be used for more than one operation. Replacements are cheap and can be fitted in a matter of seconds.

CONCLUSIONS

One of the principal advantages of this method is that the procedure does not require open surgery and that the patient's stay in hospital can be considerably reduced.

It is also easier to crack stones too large to be tackled with a cystoscopic lithotrite, and at the same time to shatter small stones, too small to be grasped easily with a blind lithotrite. In the presence of a bas fond or heavily trabeculated bladder, the vesical spark gap unit can still be brought into opposition with the stone even over a prominent prostatic middle lobe or posterior commissure hypertrophy.

The authors wish to thank Mr Bean and staff of the Genito-Urinary Manufacturing Company for their assistance with the design and construction of the instrument.

British Journal of Urology (1972), **44**, 267–273

BILATERAL SINGLE ECTOPIC URETERS

By D. Innes Williams and Robin G. Lightwood

Hospital for Sick Children, and St Peter's Hospital, London

The common form of ectopic ureter, whether unilateral or bilateral, is associated with ureteric duplication and has been very fully documented and discussed. The unilateral single ectopic ureter is less common and involves some problems in diagnosis, although no exceptional difficulty in treatment. Cases with a bilateral single ectopic ureter are, however, in a class by themselves: not only does no ureter enter the bladder in the normal situation but the bladder neck itself is never properly formed. This absence of the bladder neck involves some difficulty in classification since a reference point to which we ordinarily relate ureteric ectopia is missing, but much more serious are its implications for treatment since re-implantation of the ureters into the bladder will not alone secure continence.

Embryology.—The failure of development of the bladder neck has a simple, perhaps even a facile, embryological explanation which is illustrated in Figures 1 to 3. The normal development of the area is shown in Fig. 1. The ureteric bud arises from the elbow of the Wolffian duct where this turns forward to join that part of the cloaca which will form the urogenital sinus. The segment of the duct caudal to the elbow disappears by widening out and being incorporated in the wall of the urogenital sinus so that temporarily the normal ureter and the Wolffian duct open side by side. They later become separated because the Wolffian duct moves caudally by the formation at its extremity of a caudal and medially directed loop which is absorbed into the wall of the urogenital sinus. It then comes to open at the definitive position of the ejaculatory ducts in the male. The portion of the urogenital sinus between the orifices of the ureter and the Wolffian duct develops into the trigone and bladder neck. Figure 2 shows the development of an ectopic ureter with duplication. An accessory ureteric bud has arisen higher up on the Wolffian duct than the normal position and will thus finally open lower down in the urogenital sinus or join up with the persisting Wolffian duct orifice in the male. In this common type of ectopic ureter with ureteric duplication there is no unusual development of the bladder neck area. Figure 3 shows the situation where the ectopic ureters are single and bilateral; their openings never separate from the Wolffian duct openings and therefore there is no stimulus for the development of a trigone or bladder neck. Subsequent secondary changes may occur because the urine does not distend the bladder and it may therefore remain very small.

Pathological Anatomy.—Anatomically the deformity with which we are concerned is one in which the distal part of the urethra is normal, the bladder is small but complete. The openings of the ureters are in the urethra immediately above the verumontanum in the male, or just inside the external meatus in the female, or even further afield in the male or female genital tract. The bladder neck is never discernible as a distinct ring. Clearly there will be degrees of severity of this disorder depending upon the actual position of the ectopic orifices, upon the degree of development of the bladder and upon the abnormalities found in the upper urinary tract, for it is exceptional to find an ectopic ureter draining a normally formed kidney. Cases conforming to this description are rare: Cox and Hutch, 1966, reviewed 21 cases and Johnston, 1969, recorded a further 2. Four were males and 18 females, sex was not recorded in 1 case. This incidence is in keeping with the sex ratio of all types of ureteric ectopia (Campbell, 1963). In 2 of the males considered by Cox and Hutch there were openings into the posterior urethra, 1 into the prostatic utricle and one into the vas deferens. In those females in which the anatomy of the ureteric orifices was recorded 1 had ureters opening into the bladder, 12 opened into the urethra, 2 into the vestibule and 1 into the vagina. Two cases also had a vestibular ectopic anus. In the males the proximity of the ureteric orifices to the verumontanum emphasises their ectopic nature, but in the female there is more difficulty in classification and some, as in our Case 10 might be considered as examples of a short urethra with ill-formed bladder neck rather than as a ureteric problem.

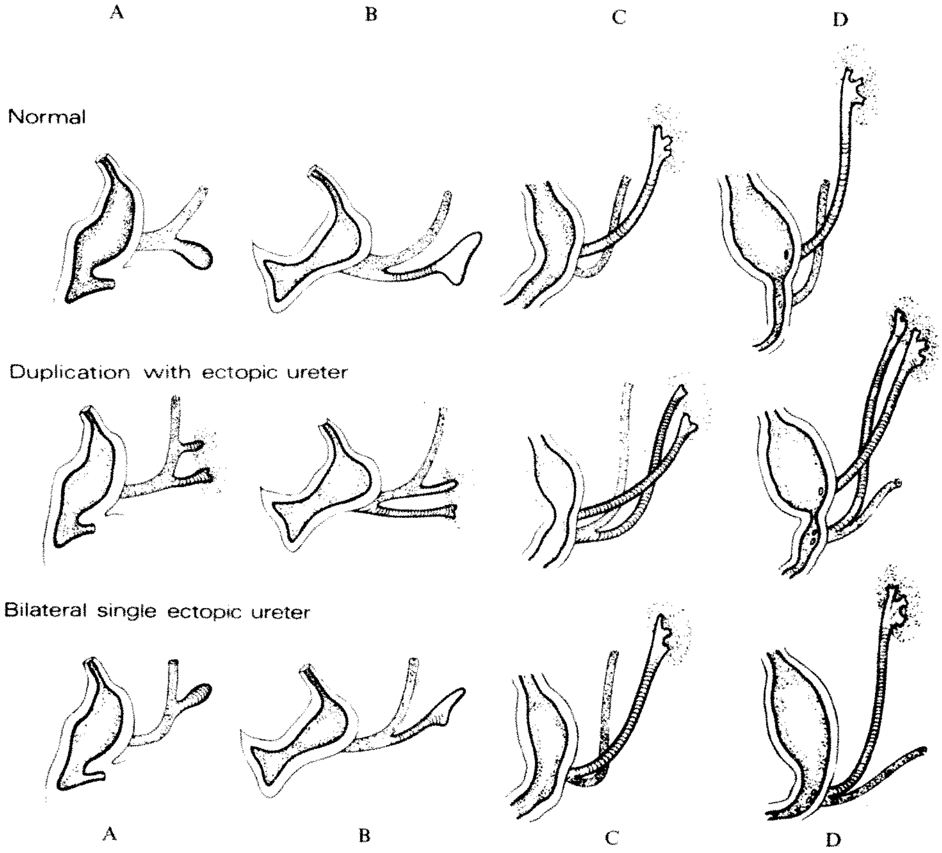

A
B
C
D
Normal
Duplication with ectopic ureter
Bilateral single ectopic ureter
A
B
C
D

FIG. 1

FIG. 2

FIG. 3

Fig. 1.—Shows the normal development. In A the ureteric bud is seen arising from the elbow on the Wolffian duct a short distance from its entrance into the urogenital sinus. In B this terminal segment is being taken up in the wall of the urogenital sinus and in C it has disappeared and at the same time the Wolffian duct is moving distally away from the ureteric orifice. In D the Wolffian duct and ureter have taken up their definitive position and in the gap between the two the bladder neck is formed.

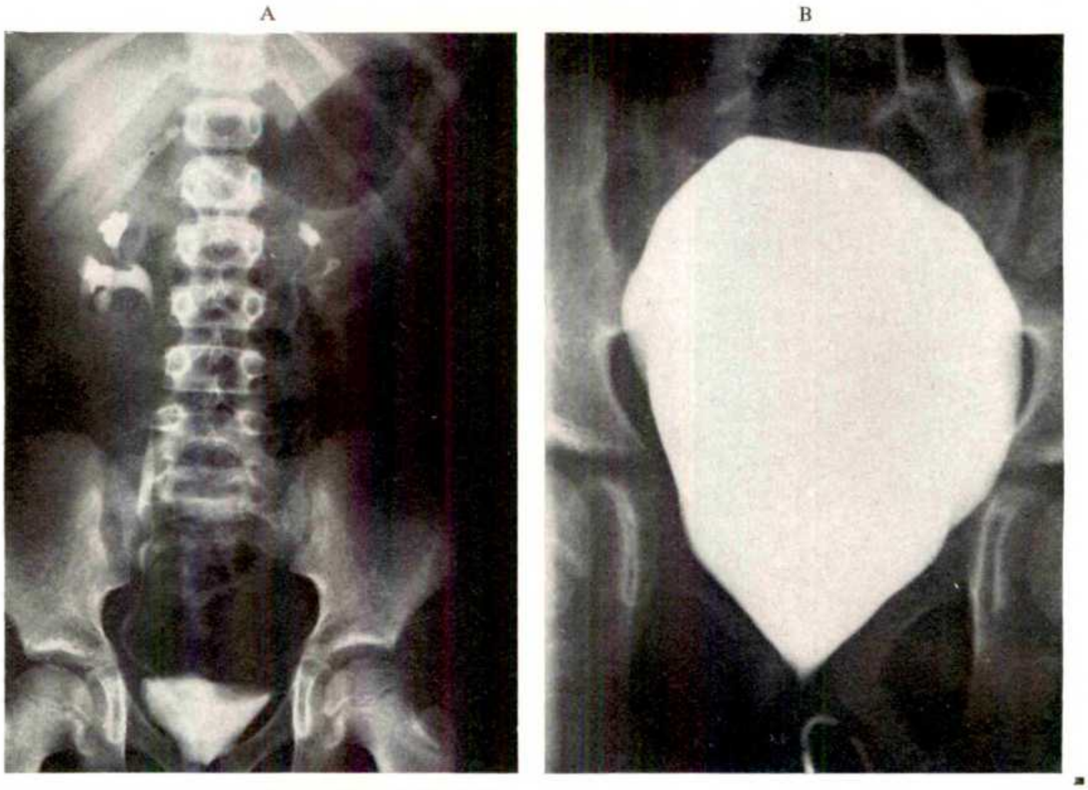
Fig. 2.—Development of an ectopic ureter with ureteric duplication. A shows the formation of accessory ureteric bud, cranial to the normal situation. In B we see the situation after the terminal segment of the Wolffian duct has been taken up into the wall of the urogenital sinus. C, The Wolffian duct has now moved caudally, carrying with it the accessory ureteric bud; the normal ureter is opening separately. In D the definitive situation of a male ectopic ureter opening into the posterior urethra, with the bladder neck formed between this and the normally placed ureter.

Fig. 3.—Development in the bilateral single ectopic ureter. A shows the formation of a single ureteric bud cranial to its normal situation. In B the terminal segment of the Wolffian duct has been taken up but the ureter still remains connected to the Wolffian duct because of its abnormally cranial situation. C, the Wolffian duct has moved distally but the ureter still joins with it at its opening. D, the definitive situation of a single ectopic ureter. There is no gap between the Wolffian duct orifice and the ureter and therefore no bladder neck is formed.

Clinical Material.—We are here concerned to report 10 additional cases of this disorder which we have personally observed. The details of the cases are set out in tabular form. One of them was an infant observed (by R. G. L.) at the University College of Rhodesia, Salisbury.

TABLE

Case	Sex	Age	Complaint	Ureteric Opening	Bladder	Reflux	Upper Tract	Operation	Result
1	M	6	Dribbling incontinence despite normal micturition.	Urethral above verumontanum.	Fair capacity.	Present.	Normal right kidney, dysplastic left.	Re-implantation of ureters, bladder neck tightening.	Continence much improved but not perfect. No reflux.
2	M	11	ditto.	ditto.	ditto.	Absent.	Fused kidneys.	ditto.	Satisfactory continence.
3	M	9	ditto.	ditto.	ditto.	Present.	Hydronephrosis right, slight dilatation left.	ditto.	Continence much improved but not perfect. Hydronephrosis less.
4	F	2 weeks	Vaginal urinary incontinence, uræmia vestibular ectopic anus.	Vagina.	Small.	Not tested.	Hydronephrosis with ureteric stenosis.	Refused.	Died at 3 months of renal failure.
5	F	6 months	Urinary infection.	Urethra, one with ureterocele.	Small.	Present.	Hydronephrotic right, small dysplastic left.	1. Re-implantation of ureters. 2. Bladder neck tightening.	Control normal after second operation but upper tract dilatation demanded diversion.
6	F	5	Total incontinence.	Urethral.	Fair.	?	Hydronephrosis right, poor function left.	Re-Implantation of ureters, tightening of bladder neck.	No improvement. Diversion advised but refused.
7	F	3	Urinary infection. Total incontinence.	Urethral.	Small.	?	Hydronephrosis right, no function on the left.	Colo-cystoplasty. Re-implanattion of right ureter, tightening of bladder neck. Lt. Nephrectomy.	Satisfactory control. Hydronephrosis remains. Requires long term chemotherapy.
8	F	3	Total incontinence.	Urethral.	Very small	?	Bilateral hydronephrosis, right ectopic kidney.	Colo-cystoplasty. Re-implantation of ureters.	No improvement, diver-diversion performed.
9	F	2	Total incontinence.	Urethral.	Very small	?	Poor function on both sides.	1. Cutaneous ureterostomy. 2. Caeco-cystoplasty with re-implantation of ureters and tightening of bladder neck.	Control improved but still inadequate. Diversion performed.
10	F	2	Urinary infection. Dribbling incontinence.	Urethral.	Fair.	Present.	Normal right. Slight pyelonephritic scarring left.	Re-implantation of ureters with bladder neck tightening.	Good control but some ureteric dilatation.



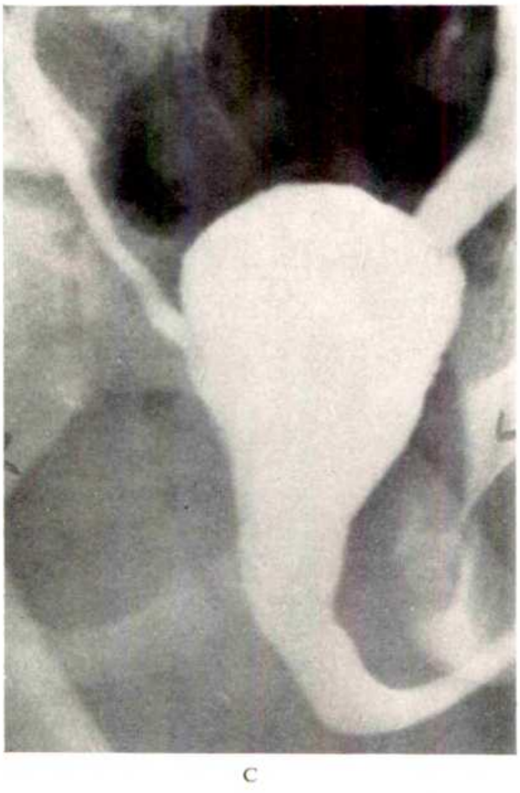


FIG. 4

Bilateral single ectopic ureter in the male.

Case 1.

A. Intravenous pyelogram showing low opening of ureters and absence of bladder neck. B. Cystogram with the bladder full, the urethra narrows down only at the level of the verumontanum. C. Micturating cystogram. Bilateral reflux is present. There is no constriction of the bladder neck in the urethra.

The remainder have been treated (by D. I. W.) at The Hospital for Sick Children or at the St Peter's Group of Hospitals in London.

The males in this series, as in other reported instances, were less common and appeared to be suffering from a less severe disorder. The 3 boys presented because of incontinence of urine which was of a continual dribbling type, worse by day than by night, although they were able to perform an act of micturition. There was no external deformity, no signs in the central nervous system and their urine was sterile. In 2 cases the upper urinary tract showed minor congenital anomalies, in the third there was a moderately severe hydronephrosis. The ureters were demonstrated to open a short distance above the verumontanum and reflux was shown in 2. The bladder neck was virtually non-existent and the bladder coned down to a relatively narrow area at the level of the membranous urethra. The bladder capacity was only a little less than average as the urine appeared to accumulate in the bladder. The situation of the ureteric orifices and the absence of bladder neck could be demonstrated radiologically (Figs. 4 and 5) and was confirmed endoscopically. In all 3 cases the ureters were implanted at a higher level and an attempt was made to

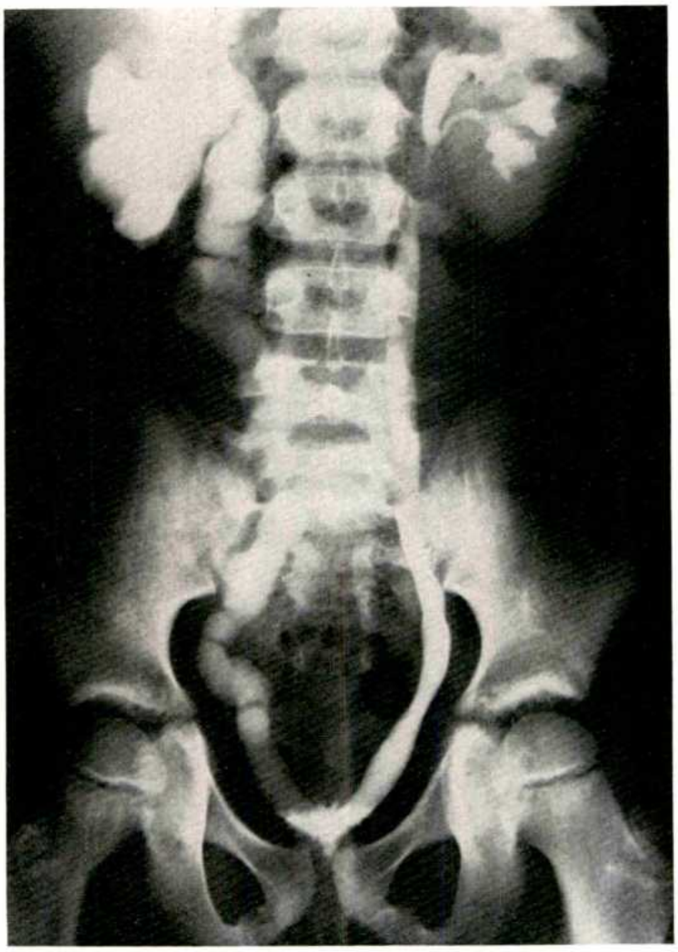
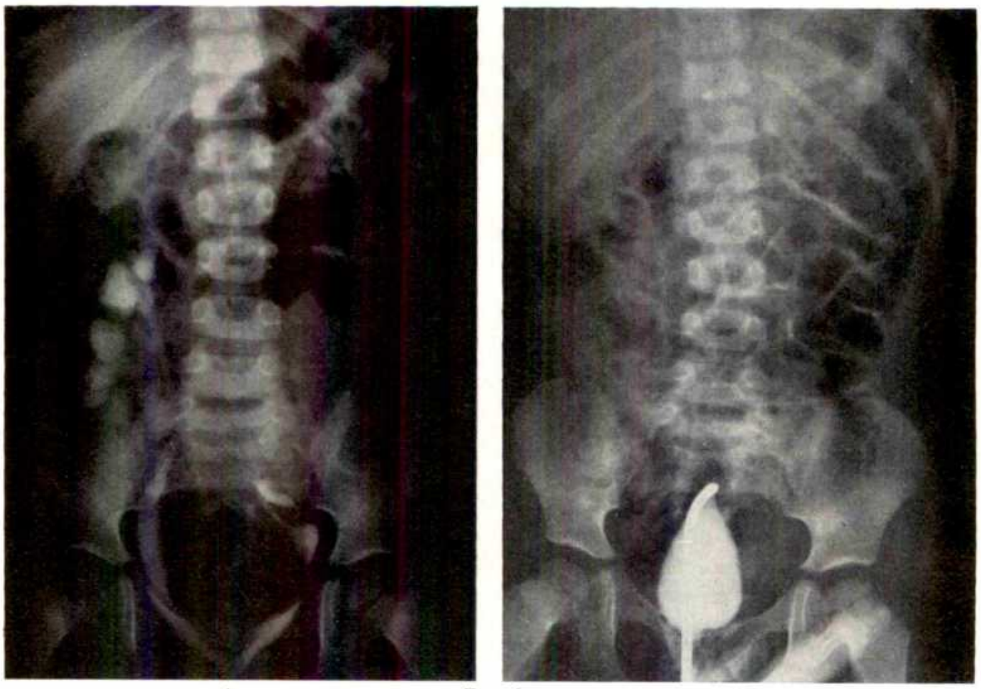


FIG. 5

Bilateral single ectopic ureter in the male. Case 3. Intravenous pyelogram showing low opening of ureters with hydronephrosis.

tighten the bladder neck by excising excess tissue on either side and uniting the muscle in a ring, as in the treatment of epispadias. One boy had a very good result, 2 had considerable improvement but did not achieve perfect continence. The upper tracts remained unchanged in 2, the hydronephrosis was improved and reflux ceased in the third.

Turning to the girls we find a very much less satisfactory situation. In all except one (Case 10) the deformity was more severe. The kidneys were grossly abnormal, either hydronephrotic or hypoplastic, the ureters were dilated and the bladder was of small capacity. As will be seen from the Table, incontinence was the usual presenting symptoms but urinary infections were also a feature of 3. In several there was a degree of renal failure. The diagnosis could usually be reached without great difficulty from the consideration of the history, the external appearance and the intravenous pyelogram. In all it was clear that the urethral orifice was normal, although there was total incontinence. In 4 children the pyelograms showed negligible filling of the bladder with ureters coming far down into the pelvis (Fig. 6). In 2 there was some bladder capacity but no bladder neck and the ureters opened a short distance above the external meatus in all, as was confirmed by endoscopy, save for the 1 post-mortem case in which a vaginal opening was found.


A FIG. 6 B

Bilateral single ectopic ureter in the female. Case 8.

A, Intravenous pyelogram shows low opening of ureters. B, Cystogram showing maximal distension of bladder while outflow partially obstructed by instrument.

In the first case treated (Case 5) the child presented at 6 months of age: she had a small left kidney with an ectopic ureterocele and a urethral ectopic ureter on the opposite side. As a first operation both ureters were re-implanted into the bladder; no improvement of continence was noted and at a subsequent operation the bladder neck was tightened. However, it was not realised at this time that reflux was present, although the bladder capacity was noted to be small. Subsequent follow-up showed that the child had gained continence but had a severely dilated upper urinary tract. The mother at first refused further treatment because of the relief of symptoms but ultimately diversion was performed. This case clearly emphasised the requirements of treatment. Firstly, a reflux preventing re-implantation, secondly, a tightening of the bladder neck and, thirdly, an increase of bladder capacity. In 3 subsequent cases the bladder was enlarged by colo- or by cæco-cystoplasty: this operation did not prove very successful, however, since it is virtually impossible to enlarge the bladder by the addition of a segment of intestine at the same time as tightening the bladder neck. Two of these children required subsequent diversion, the third acquired reasonable control. Interestingly enough the bladder itself enlarged after intestinoplasty had been performed indicating that it would probably have enlarged without this additional material. In the 2 girls where the bladder seemed large enough, re-implantation of ureters with bladder neck tightening was performed as in the boys. One became continent, although she developed some ureteric dilatation at present awaiting correction, the other remained incontinent and diversion was advised but refused.

A further case not included in this series is worthy of mention: a 3-year-old girl, sister of Case 3. She had a single left ectopic ureter opening into the urethra with an ectopic ureterocele which had ruptured spontaneously. The bladder neck was widely coned or absent, but the right ureter entered the bladder. In this case it may well have been that the ureterocele before rupture was responsible for the bladder neck deformity and, although the treatment performed was the same as in the bilateral single ectopic ureter cases, she cannot fairly be included in this category.

DISCUSSION

The incontinence which occurs in bilateral single ectopic ureters has more in common with the condition in epispadias than with that seen in the common type of ectopic ureter. The essential defect is the short urethra and incompetent bladder neck. In addition the bladder capacity is likely to be reduced. Renal and ureteric anomalies are more common than in epispadias and complicate the treatment so that in some girls urinary diversion is the only appropriate therapy. The reconstructive procedure attempted in this series has been, in essence, the operation described by Young (1937) for epispadias. The ureters have been re-implanted at a higher level and an attempt has been made to form from the bladder base a long muscular tube. The results have been variable, as in epispadias itself, and success or failure seems more related to the severity of the condition than to the operative technique.

We wish to thank Mr Raymond Weinberg, Department of Surgery (Urology), University College of Rhodesia, for allowing us to include Case number 4.

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ABSTRACTS FROM CURRENT UROLOGICAL LITERATURE

American Journal of Roentgenology

By B. H. Page

" Roentgen Features of Reflux into the Prostate, Seminal Vesicles and Vasa Deferentia." H. A. Mitty. (1971, **112,** 603-606.)—A radiologist from the Mount Sinai Hospital, New York, describes the X-ray appearances of reflux into the prostatic ducts, seminal vesicles and vasa deferentia. He says that " reflux of this type is best demonstrated by voiding cysto-urethrography performed at the end of intravenous urography " but all except one of his illustrative films are produced by the initial introduction of medium directly into the bladder or urethra. The conditions showing these features are chronic prostatitis (in which the prostatic ducts become dilated) and following prostatectomy. Urethral stricture is another important cause of reflux into the prostatic ducts.

" Pelvi-calyceal Extravasations." F. Lopez. (1971, **112,** 593-599.)—The author, a radiologist at the Montfiore Hospital, New York, describes 6 cases of extravasation of the following types. 1. Acute ureteric obstruction (a stone was suspected but not demonstrated). 2. Chronic ureteric obstruction due to enlargement of the prostate (the patient also had generalised lymphosarcoma). 3. Penetrating injury (stab wound) causing laceration of the renal pelvis. 4. Non-penetrating injury of the kidney. 5. " Lateral flexion injury ". A boy of 10 was struck in the left flank by a car and sustained complete severance of the uretero-pelvic junction. 6. Surgical trauma, illustrated by extravasation from a calyx following the unroofing of a solitary renal cyst. The diagnosis in all these cases was made mainly by excretion pyelography which may show the ureter as a translucent line running through the extravasated medium. With regard to treatment, the author notes that spontaneous extravasation usually recovers quickly without intervention, but that in many cases of post-traumatic extravasation surgical treatment is needed.

" Prostatic Metastasis to the Base of the Skull Simulating Meningioma en Plaque." J. R. Kirkwood, M. T. Margolis and T. H. Newton. (1971, **112,** 774-778.)—4 cases of metastatic invasion of the base of the skull by prostatic carcinoma are reported by radiologists from the University of California School of Medicine, San Francisco. In 3 of the cases the primary disease had already been diagnosed (from 7 years to 18 months previously) but in the 4th the prostatic carcinoma was discovered only after the secondary manifestation. In all 4 cases the diagnosis was established by biopsy or at autopsy. The 2 main symptoms of the metastasis were progressive exophthalmos and deterioration of vision. X-ray showed hyperostosis of the base of the skull, which is also found in " meningioma en plaque ", in fibrous dysplasia and in some cases of reaction to adjacent paranasal chronic inflammatory disease. These various causes may be differentiated by clinical and other studies, but the authors point out 2 radiological features particularly noted in the cases of metastatic prostatic carcinoma.—involvement of the zygoma (never found in meningioma) and the absence of encroachment on the optic foramen.

Annals of Surgery

By A. R. C. Higham

" Effect of Acute Renal Failure upon Cell Division in the Jejunum: Radioautographic and Ultrastructural Studies in the Mouse." F. T. McDermott, J. Nayman, and W. G. R. M. de Boer. (1971, **174,** 274-282.)—The effect of acute renal failure upon cell division in the crypts of Lieberkühn of the jejunum was investigated by radioautography with tritiated thymidine in mice. Acute renal failure was induced in different groups by intraperitoneal injection of the nephrotoxic agent uranyl nitrate or by urinary obstruction. Cell division was inhibited in both groups and was most pronounced with severe renal failure.

" Respiratory Failure Complicating Post-Traumatic Acute Renal Failure." J. E. Zimmerman. (1971, **174,** 12-18.)—Respiratory failure was frequently encountered in patients with post-traumatic renal failure. It was difficult to evaluate the role of overhydration. When this cannot be ruled out as the cause of respiratory failure, extracorporeal haemodialysis should be utilised.

" Operative Blood Flow Measurement in Transplanted Human Kidneys and Subsequent Rejection." S. E. Bergentz, U. Brunius, L. E. Gelin and D. H. Lewis. (1971, **174,** 44-47.)—In 66 cadaver kidney transplants, renal blood flow at the time of transplantation was significantly lower in those kidneys that later had severe rejection episodes.

" Effect of Ethacrynic Acid and Frusemide on Renal Function in Hypovolemia." A. A. Stone and W. M. Stahl. (1971, **174,** 1-11.)—Controlled haemorrhage was produced in 14 dogs and in 4 normal human volunteers. Both drugs proved capable, in the hypovolaemic state, of producing large increases in urinary volume, urinary sodium excretion and osmolar clearance, i.e. the total effect of these drugs is to improve renal function.

" Prevention of Urological Complications after Kidney Transplantation." R. Weil, III, R. L. Simmons, M. B. Tallent, R. C. Lillehei, C. M. Kjellstrand and J. S. Najarian. (1971, **174,** 154-160.)—The incidence of urological complications following kidney transplantation at the University of Minnesota has been reduced from 19% in the first 100 transplants to 3% in the last 100 transplants (January, 1968-May, 1970). Pyelo-ureterostomy has been followed by urinary leak or obstruction in a high percentage of cases. Uretero-neocystostomy has resulted in no urological complications in the primary transplants done since January of 1968.

The Australian and New Zealand Journal of Surgery

By H. H. Pearson

"**Deviation of the Ureters due to Giant Bladder Diverticula.**" Rodney R. A. Syme. (1971, **41**, 62-64.)—From the Austin Hospital Melbourne the author describes a patient aged 73 years with obstruction from a fibrous prostate, urinary retention and massive thin walled diverticula which had elevated the peritoneum in the rectovesical pouch and elevated and displaced the ureters. The patient died of pulmonary embolism following cystography, and the bladder, diverticula, prostate and lower ureters were removed at autopsy. The left ureter lay lateral to the larger left diverticulum at the pelvic brim. No mention of lateral deviation of the ureter caused by a diverticulum could be found in the literature. The right ureter was displaced medially by a large right diverticulum. The author discusses the differential diagnosis of lateral and medial deviations of the ureters, and the aetiology of diverticula and their relationship to obstruction. He elaborates too on the preservation of kidney function in the presence of chronic urinary retention in the presence of diverticula—Hamilton's safety-valve theory. In his patient the blood urea was only 42 mg. per 100 ml.

"**Inverted Papilloma of the Urinary Bladder: A Report of Two Cases.**" J. J. Sullivan, J. G. Watson, C. W. Kingston, and R. P. Yaxley. (1971, **41**, 60-62.)—A distinctive variety of bladder papilloma with a characteristic histology was first described by Potts and Hirst (1963) to which they gave the name "inverted papilloma". 3 further cases were reported by Trites (1969) and similar tumours have been seen by Trites in Vancouver and by Hirst (1970) in Sydney. The authors report 2 cases from Brisbane, Queensland. One was discovered as a separate tumour entity during a prostatectomy, and the other presented with haematuria and was found to have a solid pedunculated tumour at the bladder base. The characteristic histology of the lesions is that of a reversal of the usual papilloma pattern. There is a surface layer of transitional cells with a downgrowth of strands of similar epithelium into the stroma. Cavities are commonly present in anastomosing cords and contain amorphous eosinophilic material. Squamous metaplasia may be present. The authors stress that such tumours are readily recognisable by the pathologist and should be borne in mind by the urologist as there is a risk of their being mistaken for infiltrating carcinoma. All evidence at present points to a benign clinical course and examples so far published have arisen from the region of the prostatic urethra or adjacent bladder neck. No comment is made as to the significance of the eosinophilic material.

"**Nephrocolic Fistula: Report of a Case.**" E. Vlahakis, J. J. Bucchiere Jr. and F. J. Leary. (1971, **41**, 58-59.)—Approximately 100 cases of nephrocolic fistula have been reported in the literature. From the Mayo Clinic the authors report a further case. A 59-year-old female presented with recurring urinary infection. A left retrograde pyelogram showed a chronic pyelonephritis with filling of the colon near the splenic flexure. Barium enema revealed a fistulous track arising from the descending limb of the splenic flexure. At operation there was found a small pyelonephritic kidney with a chronic abscess cavity between it and the splenic flexure of the colon. A nephrectomy was performed and the fistulous opening into the colon oversewn. The authors comment that the pathological condition in nephrocolic fistula is almost always in the kidney and that tuberculosis, non-specific infection and calculi are the common causes. Modes of presentation include recurring urinary tract infection, pneumaturia, diarrhoea and discharge of calculi. The best diagnostic aid is retrograde pyelography, and treatment usually entails nephrectomy with closure of the fistula or partial colectomy.

British Journal of Radiology

By A. R. C. Higham

"**Is Retroperitoneal Fibrosis a Self-Limiting Disease?**" F. W. Wright and R. C. Saunders. (1971, **44**, 511-514.)—2 cases of retroperitoneal fibrosis are presented in which only 1 ureter was freed from the fibrosis at operation. In both cases the contralateral kidneys, which were also partially obstructed, showed remission of the disease, in one case with hypertrophy of the kidney and in the other with atrophy. Another case with bilateral spontaneous remission of obstruction is cited.

"**The Urinary Tract Anomalies Associated with Agenesis of the Abdominal Wall.**" J. Cremin. (1971, **44**, 767-772).—The triad of lesions usually noted in the syndrome are: absent abdominal muscles, undescended testes, and urinary tract anomalies; with atrophic kidneys, dilatation of the ureters and bladder, and dilatation of the posterior urethra. 8 cases are described, of which 5 died.

"**The Use of Ultrasound in the Diagnosis of Renal Disease.**" R. A. Mountford, F. G. M. Ross, R. J. Burwood and M. S. Knapp. (1971, **44**, 860-869.)—Ultrasound may be of value when excretory urography has failed to demonstrate a nephrogram; it has a place in the differentiation between solid and cystic renal masses; it may provide clinically useful information when radiography is contra-indicated, viz. in pregnancy; and the ultrasonic appearances in polycystic disease are characteristic. The results of 42 scans are analysed and an accuracy of diagnosis of 80% was achieved.

"**Osteogenic Sarcoma with Calcified Renal Metastases.**" J. A. Nelson, R. E. Clark and A. J. Palubinskas. (1971, **44**, 802-803.)—These were multiple metastases found 3 years after amputation above the left knee.

"**The Renal Cortical Angiogram and Renal Blood Flow: Studies of Renal Cortical Perfusion under Differing Functional States.**" J. P. Lavender and T. Sherwood. (1971, **44**, 505-510.)—Fine detail angiograms of the renal cortex were compared with renal blood flow as the aortic pressure was dropped in 7 dogs by simple aortic occlusion and by bleeding. Angiograms were also obtained in other dogs under conditions of normal and zero blood flow during renal artery constriction; and in death. The renal cortical vascular bed can remain in a normal state with no renal blood flow at all. By contrast, marked vasoconstriction occurs early in haemorrhagic hypotension with only moderate falls of perfusion pressure and renal blood flow. It is concluded that the perfused glomerular territory bears no relation to total renal blood flow. The static angiogram is valuable in revealing vascular behaviour at any moment, but cannot be used to assess flow.

"Arterial Hypertension and Position of the Kidneys—An Angiographic Study." I. Garri, C. Sirken and H. Salinger. (1971, **44**, 682-685.)—The level of origin of the renal arteries is shown to be significantly higher in hypertensive patients.

"Ultrasound in the Investigation of Space Occupying Lesions of the Urinary Tract." E. Barnett and P. Morley. (1971, **44**, 733-742.)—The demonstration of the consistency of a renal mass is of vital importance in the differential diagnosis between a neoplasm and a cyst or hydronephrosis, and this information can usually be obtained with sonar. The differentiation between gross hydronephrosis and a unilocular cyst may not be possible unless normal renal tissue can be demonstrated. The size and exact location of a bladder neoplasm can be shown, though difficulty may be experienced with small capacity bladders and anterior wall masses. The use of ultrasound offers a distinct contribution to the investigation of the urinary tract: it is complementary to other diagnostic procedures.

"The Use of Radioactive Hippuran in the Management of Cadaveric Renal Transplants." R. A. Branch, G. A. Coles, A. Eynon, G. R. Jones and E. Lowder. (1971, **44**, 697-704.)—The use of a radiohippuran clearance and renography with blood background subtraction in 35 recipients of a cadaveric renal transplant is described. The presence of renal blood flow during the initial oliguria can be demonstrated by this technique. The renogram during the post-operative period of acute tubular necrosis usually continues to rise until 30 minutes and no peak is seen. After diuresis most patients are found to have a normal renogram and to have a significant rise in radiohippuran clearance. Characteristic abnormalities may be seen with acute and chronic rejection or urinary obstruction and these abnormalities are reversed if treatment is successful. There are still limitations to the use of renography in the diagnosis of acute rejection or obstruction during the initial oliguria. The combined test is of value in the management of cadaveric renal transplantation.

Deutsche Medizinische—ochenschrift

By John Grieve

"The Diagnosis and late Results of Surgical Treatment of Hypertension due to Renal Artery Stenosis." F. W. Lohmann, T. Dissmann, R. Gotzen, M. Molzahn, W. Oelkers, G. Rücker, H. Baumgartel and D. Bachman. (1971, **96**, 1347-1356.)—A group of 34 hypertensives ranging in age from 18 to 65 years was operated on for renal artery stenosis. Of these 18 had a nephrectomy, 1 a heminephrectomy and the other 15 a bypass or patch operation. The result was cure in 11, improvement in 15 and no change in 8. Secondary aldosteronism was of great prognostic significance particularly in the older patients. A rise in peripheral renin concentration particularly venous and on the side of the stenosis indicated at least improvement and probably cure of the hypertension post-operatively. In those under 50 years a short history and raised renin were favourable signs for cure. In elderly patients hypotensive drugs should be used enthusiastically before operation is even contemplated. This is particularly important if the stenosis is bilateral.

Journal of the American Medical Association

By D. T. H. Paine

"Retroperitoneal Lymphadenectomy for Testicular Tumors." P. Walsh, J. J. Kaufman, W. F. Coulson, and W. E. Goodwin. (1971, **217-3**, 1953-1966.)—64 patients have been followed by the Department of Surgery and Urology, UCLA and Woodsworth Veterans Hospital, Los Angeles, for 3 years after radical lymphadenectomy for testicular germ-cell tumours, other than seminoma. Freedman and Moore's classification has been used. Survival rates in stage A terato-carcinoma and embryonal carcinoma were 93% and 94%; but with stage B tumours, survival rates for terato-carcinoma were 77%, and for embryonal carcinoma were 29%. The effect of radiotherapy was not defined. There was no apparent advantage in doing bilateral lymphadenectomy as opposed to unilateral.

"Alkylating Agents and Human Spermatogenesis." D. G. Miller. (1971, **217-12** 1662-1665.)—Working at the Memorial Hospital for Cancer in New York and the Strang Clinic, Dr. Miller has investigated spermatogenesis in 11 patients with malignant lymphoma treated with maintainence doses of the alkylating agents chlorambucil or cyclophosphamide. All the patients developed azoospermia. 1 patient was investigated 1 year after cessation of treatment; he had no return of spermatogenesis.

"Hemodialysis and Transplantation in Adults with Polycystic Renal Disease." J. M. Lazarus, G. L. Bailey, C. L. Hampers and J. P. Merrill. (1971, **217-13**, 1821-1824.)—Experience at the Peter Bent Brigham Hospital since 1960 were reviewed. There were 36 patients with renal failure due to polycystic disease who were placed on the dialysis-transplant programme. These patients were particularly prone to haematuria and pyelonephritis and occasionally required bilateral nephrectomy. Generally speaking, non-nephrectomized patients maintained higher haematocrit values than did patients with other causes of renal failure. Their post-operative courses resembled those of other transplant cases.

"National Transplant Communications Network." P. I. Terasaki, G. Wilkinson, and J. McClelland. (1971, **218-11** 1674-1678.)—These workers describe the present network for pooling information for cadaver kidney transplant sharing in the United States of America and Canada. Although the information given is incomplete to my own knowledge in regard to Canada, the article points out the advantages of a large pool of recipients. The expected rise in the number of Group O waiting recipients is confirmed. This is due to the use of type O kidneys for type A or B recipients. At the time of reporting, there was a total of 864 waiting recipients from 61 transplant centres with information on the computerized file. At that time a total of 215 kidneys had been exchanged on the network.

La Presse Medicale

By JOHN GRIEVE

"**Hypertension Rénovasculaire.**" A. FOURNIER. ((*a*) 1971, **79**, 903-910, (*b*) 1971, **79**, 1209-1219, (*c*) 1971, **79**, 1715-1721.)—In these 3 articles the whole subject of renovascular hypertension is reviewed. Particular attention is given to the many different tests which have been and are employed in the assessment of these patients. Assessment remains difficult because of disparities between the results of different tests. Treatment continues to be uncertain and the ultimate results are assessed more often by the general circulatory state rather than by the local renal changes. There is an extensive bibliography and these articles are well worth study by all interested in this field.

"**Renal Allotransplantation in Man: Report of 72 cases.**" R. KÜSS, M. LEGRAIN, J. C. GLUCKMAN, J. GUÉDON and J. POISSON. (1971, **79**, 1889-1894.)—This group from Paris report 72 renal allotransplants in 67 patients performed between 1st January 1965 and 1st September 1970. Cadaver kidneys were used in 44 patients. Over the whole period the 2-year survival rate was 77% where the donor was related and 53% when no relationship existed. In the last 3 years the corresponding survival rates among 51 patients were 87% and 62% respectively. The number of rejection crises was greater where the degree of histocompatibility was less. ALG administration did not show obvious benefits. The improved results are attributed to greater experience of all stages of transplantation and better use of the non-specific methods of immuno-suppression.

"**The Practical Value of Alpha-Foetal-Protein in the Diagnosis and post-operative Follow-ups of Embryonic Tumours of the Testis.**" C. BOURGEAUX, F. MARTIN, F. CABANNE, P. AUPECLE and J. GUERRIN. (1971, **79**, 1589-1590.)—This group in Dijon examined the serum of 12 patients with testicular tumours for the presence of alpha-foetal-protein (A.F.P.) and found the protein in 2 patients. Both these patients had embryonic carcinoma. Removal of the primary was followed by a fall in the amount present. In one of the patients the amount later increased and despite therapy widespread metastases appeared with further increase in the amount of A.F.P. In the other the level fell after operation but not as much as expected. Metastases were again found but excision and cobalt radiation were followed by apparent cure. These findings suggest that estimation of A.F.P. may be of both diagnostic and prognostic value in embryonic carcinoma.

Surgery, Gynaecology and Obstetrics

By THOMAS MOORE

"**Stratification of Oxygen in the Canine Kidney.**" HARRY C. MILLER. (1971, **132**, 1025-1029.)—Working with mongrel dogs in the University of Rochester, New York, the author measured the oxygen tension in canine kidney tissue by the use of a platinum probe. Contrary to previous workers, he always found the oxygen tension highest in the cortomedullary region, next in the cortex and lowest deep in the medulla. The actual levels, however, were very variable from one dog to another and from one part of the kidney to another. The method, therefore, can have no scientific value in the clinical field.

"**Treatment of Advanced Carcinoma of the Prostate.**" CLYDE E. BLACKARD. (1971, **133**, 97-98.)—This editorial is an official statement of the Veterans Administration Urological Research Group. The author reiterates the findings as previously published by the Group, on the high death rate from cardiovascular disease of cases of carcinoma of the prostate treated with a daily dose of 5 mgs. of diethystilboestrol. A new trial has now been started with a daily dose of 1 mg. of the same oestrogen; this appears to be as effective in controlling the malignant disease, but also in lowering the cardiovascular complications. Investigations into the effects of oestrogens on blood clotting, sodium retention and lipid metabolism are being pursued.

"**Low Flow Hypothermic Renal Perfusion.**" LUIS GRANA, W. L. DONNELLAN and ORVER SWENSON. (1971, **133**, 401-413.)—As a result of many detailed and ingenious well-controlled experiments performed on dogs in the Northwestern University School of Medicine in Illinois, Chicago, the authors have shown that considerable protection against renal ischaemia is provided by perfusion of cold blood at the slow flow rate of 15 ml. per minute to maintain a core temperature of 15 to 20 degrees C. and a pO_2 value above 150 mm. of mercury. As a result of these studies, a practical method for the preservation of cadaver kidneys for up to 8 hours has been developed.

"**The Evaluation of Pudendal Nerve Block by Measurements of Urethral Pressure.**" SHLOMO RAZ and MARCO CAINE. (1971, **133**, 453-457.)—In the Hadassah University Hospital, Jerusalem, the authors have used urethral pressure profile studies to test the effectiveness of pudendal nerve anaesthetic block and its effect on micturition. Where it has been successful, permanent section of the nerve or nerves has been carried out. Of 15 cases studied, 2 are reported in more detail.

"**The Surgical Treatment of Renal Artery Embolism with Anuria.**" M. LACOMBE. (1971, **133**, 419-424.)—From the Hospital Beaujon, Paris, the author reports 3 cases of renal arterial embolism. As is usual, the diagnosis was made late in all, and preoperative dialysis was necessary. 2 cases recovered and 1 died after operation. In both those who recovered, some degree of renal dysfunction persisted. The author discusses the clinical picture of the conditions, common causes, the investigation and treatment. Only 14 other cases have been recorded in the literature.

"**Rectal Flap Repair of Prostatorectal Fistula.**" FRANCIS A. BENEVENTI and WILLIAM H. CASSEBAUM. (1971, **133**, 489-492.)—From the Joseph McCarthy Urological Department and Department of Surgery, the French and Polyclinic Medical School and Health Center, Inc., New York, the authors present their method of treatment of prostato-urethral rectal fistula. In a very difficult case, they have exposed the fistula by the splitting of the anal sphincter and rectum posteriorly. Instead of attacking the fistula direct, they have cut a flap about 4 cms. wide, surrounding the fistula right through the rectal wall. They have freed this flap as a cuff, removed the mucosal surface, and then sutured the remaining muscle in one layer as a plug to close the fistula. They have then closed the anterior rectal wall, behind the fistula, and closed the wound in the usual way. In 1 case, which had resisted 4 previous attempts at closure, this method was successful.

Der Urologe

By John Grieve

"Neurogenic Bladder Disturbances in Children with Meningomyelocele." H. J. Pompino, M. Westenfelder and H. Fendel. (1971, **10**, 213-218.)—In 1968 42 children aged 8 months to 7½ years with meningomyelocele were reviewed. Of these 38 had operations for thoracic, lumbar or sacral lesions and all of these had bladder disturbances. Classification by the Bors method was possible in 17. In many of the children the detrusor showed contractile and paretic features. Urinary tract infection can be controlled in many of them but it is very important to relieve by medical or surgical means any obstruction which interferes with bladder emptying.

"Analysis and Significance of Urinary Calculi containing Magnesium." C. Maurer and B. Meier. (1971, **10**, 158-161.)—In this chemical study from Heidelburg the authors show that qualitative analysis of urinary stones is inadequate for classification. Over the past 2 years 644 stones have been analysed quantitatively. Quantitative analysis using appropriate techniques gives information about the amounts of the individual minerals and about the types of compound present in the stones. When uric acid, phosphate and ammonium occur at the same time estimation of magnesium can clarify in which compound the ammonium ion occurs. Recurrent calculi are more frequent when the primary stone contains magnesium and this information is of value in treatment and prophylaxis.

"Investigations on Urinary Acidification with Drugs." H. Sommerkamp and L. Weihe. (1971, **10**, 145-151.)—In 17 patients with alkaline urinary infections and 10 normal controls, ascorbic acid, hydrochloric acid and ammonium chloride were used to acidify the urine. When effectiveness, relative absence of side effects and cost were considered, hydrochloric acid was the most useful drug for long term treatment. This was administered as Acidol-Pepsin tablets in a dose of 3 tablets thrice daily. Each tablet was equivalent to a dose of 16 drops of dilute hydrochloric acid.

"Stone Analysis by the Crystallisation Method." M. Marscek and P. Burchardt. (1971, **10**, 154-158.)—These workers from Hamburg claim that this technique of crystallisation gives an exact qualitative and quantitative way for analysing urinary calculi. Using differential solubility the stone-forming elements are separated by re-crystallisation. The crystals are then recognised and counted microscopically. The results in 350 analyses are given. The method appears valuable for routine use in urological practice.

Urologia Internationalis

By John Grieve

"Autoradiographic Demonstration of 3 Hydroxyanthranilic Acid (^{3}H) in the Urinary Bladder of Rats before and after Bilateral Nephrectomy—a Contribution to the Etiology of Bladder Carcinoma." K. Hochberg, W. Kochen, L. Rohl and A. Porep. (1970, **25**, 502-510.)—In 64 rats after bilateral nephrectomy and 70 rats without operation 3-hydroxyanthranilic acid (^{3}H) was injected intraperitoneally and this gave a characteristic autoradiographic distribution. In the unoperated group there was a very pronounced increase in radioactivity in relation to the bladder epithelium suggesting that the principal route for excretion of tryptophan metabolites is through the kidney. This high concentration of potentially carcinogenic metabolites on the bladder epithelium may play a role in carcinogenesis.

Urologija i Nephrologija

By Victor Lane and Anton Pytel

"Cystectomy in Patients with Bladder Carcinoma." N. A. Lopatkin and V. M. Krendel. (1970, **4**, 37.)—Total cystectomy for carcinoma was carried out on 33 patients in the 2nd Moscow Medical Institute between 1954 and 1968. Having reviewed the various forms of urinary diversion, the authors conclude that ureterosigmoidostomy is the method of choice in association with cystectomy because of the reduced mortality and complication rates involved.

"Partial Nephrectomy for Carcinoma of a Solitary Kidney." V. S. Ryabinsky and L. E. Ivanova. (1970, **5**, 42.)—A woman of 61 with a solitary kidney presented with a 2-month history of diffuse haematuria. In hospital, periods of anuria, due to obstruction of the ureter by clots, developed which required treatment by ureteric catheterisation. When the solitary left kidney was explored, a carbuncle, 1½ cm. in diameter, was found in the lower pole; this was excised. Pre-operative X-rays had suggested a neoplasm affecting the upper calyx and this was confirmed by splitting that section of the kidney. Having confirmed the diagnosis by biopsy, the upper pole of the kidney was resected. Episodes of temporary renal failure occurred during the first 2 months post-operatively but 1 year afterwards the patient was well with satisfactory renal function.

"Surgical Treatment of Stress Incontinence in Women." G. L. Aleksandrovich and G. A. Antonov. (1971, **4**, 29.)—Using the Marshall-Marchetti procedure, good results were achieved in 22 out of 24 women with stress incontinence. The technique is simple and free of complications and, apparently effective even in the elderly.

"Perforation of the Ureter in Removal of Stones with the Dormia Extractor." Z. Kh. GOGICHAEV and G. D. ORLOVA. (1971, **4**, 66.)—A stone measuring 0·8×0·6 cm. had remained in the lower ⅓ of a female patient's right ureter for 1 year. A Dormia extractor was felt to pass the stone at 7 cm. but was held up at 15 cm. It was impossible to open the basket and X-ray studies confirmed that the ureter had been perforated. The extractor and the stone were removed by open operation.

"A Rare Anomaly of the Ureter in a 3½ year old Child." O. A. TROITSKY. (1971, 4, 64.)—A second ureter was found leading from the pelvis of the pyelonephritic upper segment of a duplex right kidney. This ureter ran behind the inferior vena cava at the level of the 2nd lumbar vertebra emerging between the cava and the aorta and ended blindly on the anterior surface of the cava. The upper segment of the kidney was removed, together with the ureter, which was divided just as it passed behind the inferior vena cava. This child had presented with attacks of abdominal pain accompanied by pyrexia and increased frequency. The preoperative diagnosis, based on pyelography, was of a renal or ureteric tumour.

Zeitschrift für Urologie

By JOHN GRIEVE

"Investigation of the Serum and Urine Content of Magnesium in Patients with Urinary Calculi." B. TERHORST and W. LÜBKE. (1971, **64**, 649-655.)—In 100 normal individuals and 330 patients with urinary calculi the magnesium level in urine and serum was measured and correlated with the calcium level. In 30% of the stone formers there was a reduced amount of magnesium in the urine but a normal amount of calcium. Increased calcium was present among 38% of the patients. It is possible that there may be a defect in magnesium absorption and this might be helped by oral treatment with magnesium preparations.

NEWS FROM HOME AND OVERSEAS

THE UROLOGICAL ASSOCIATION OF SOUTH AFRICA

The Biennial Congress of the South African Urological Association will be held in the Kruger National Park from 7th to 11th August 1972. Particulars may be obtained from: Dr V. E. Hesse, 702 Nedpark Medical Centre, Sunnyside, Pretoria, South Africa.

POLISH UROLOGICAL SOCIETY

The XIIIth Scientific Conference of the Polish Urological Society will be held on 9th, 10th and 11th of June 1972 in Lublin, Poland. Further details from: Komitet Organizacyjny, XIII Naukowego Zjazdu Polskiego Towarzysta Urologicznego, Klinika Urologiczna A.M. w Lublinie, ul. Jaczewskiego 8.

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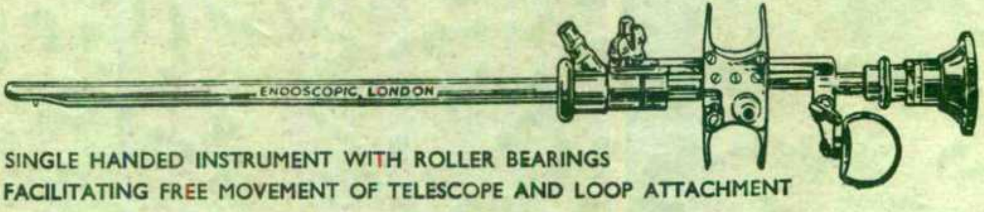

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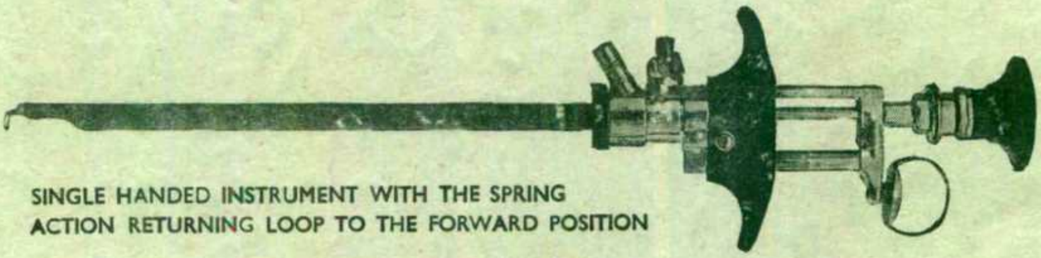

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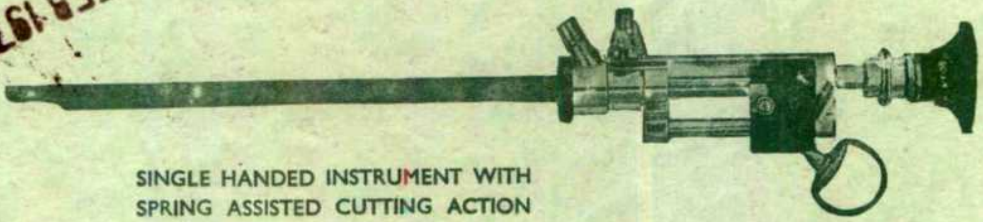

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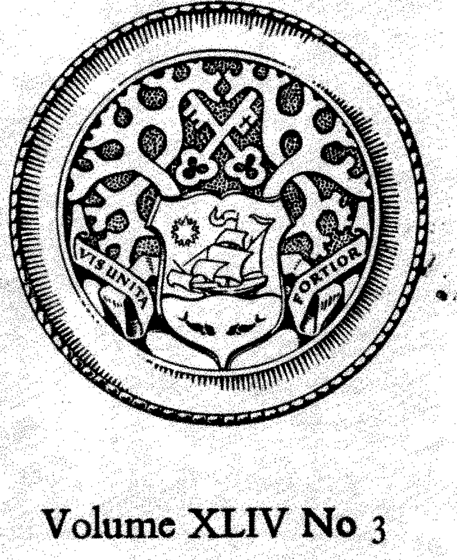

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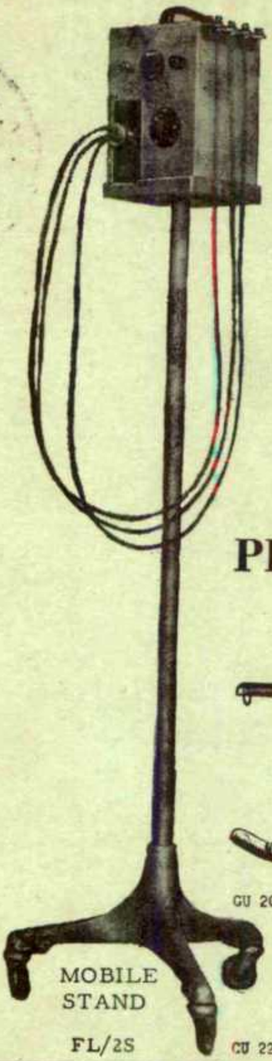

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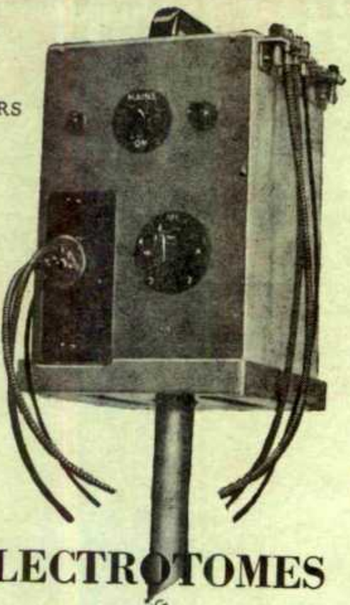

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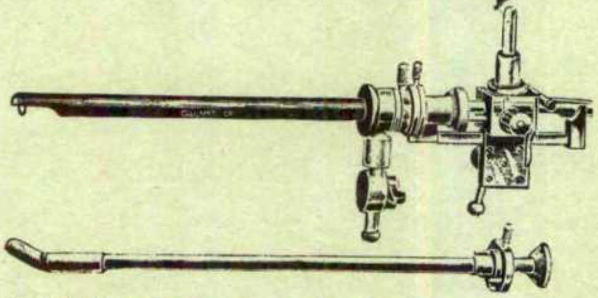

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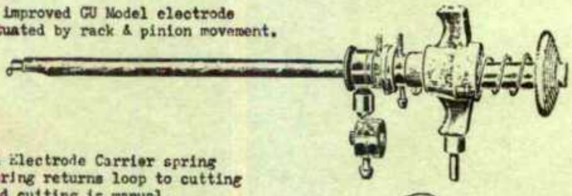

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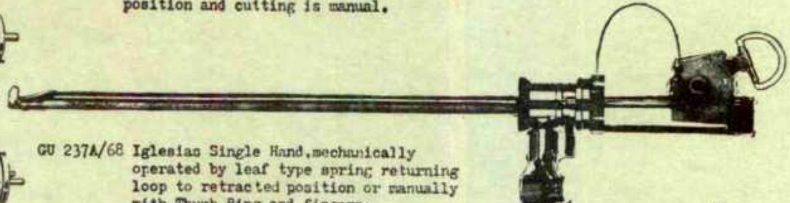

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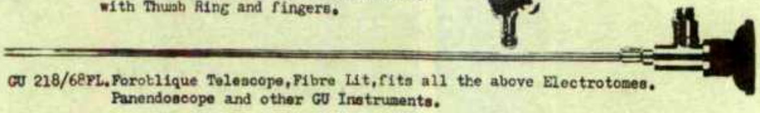

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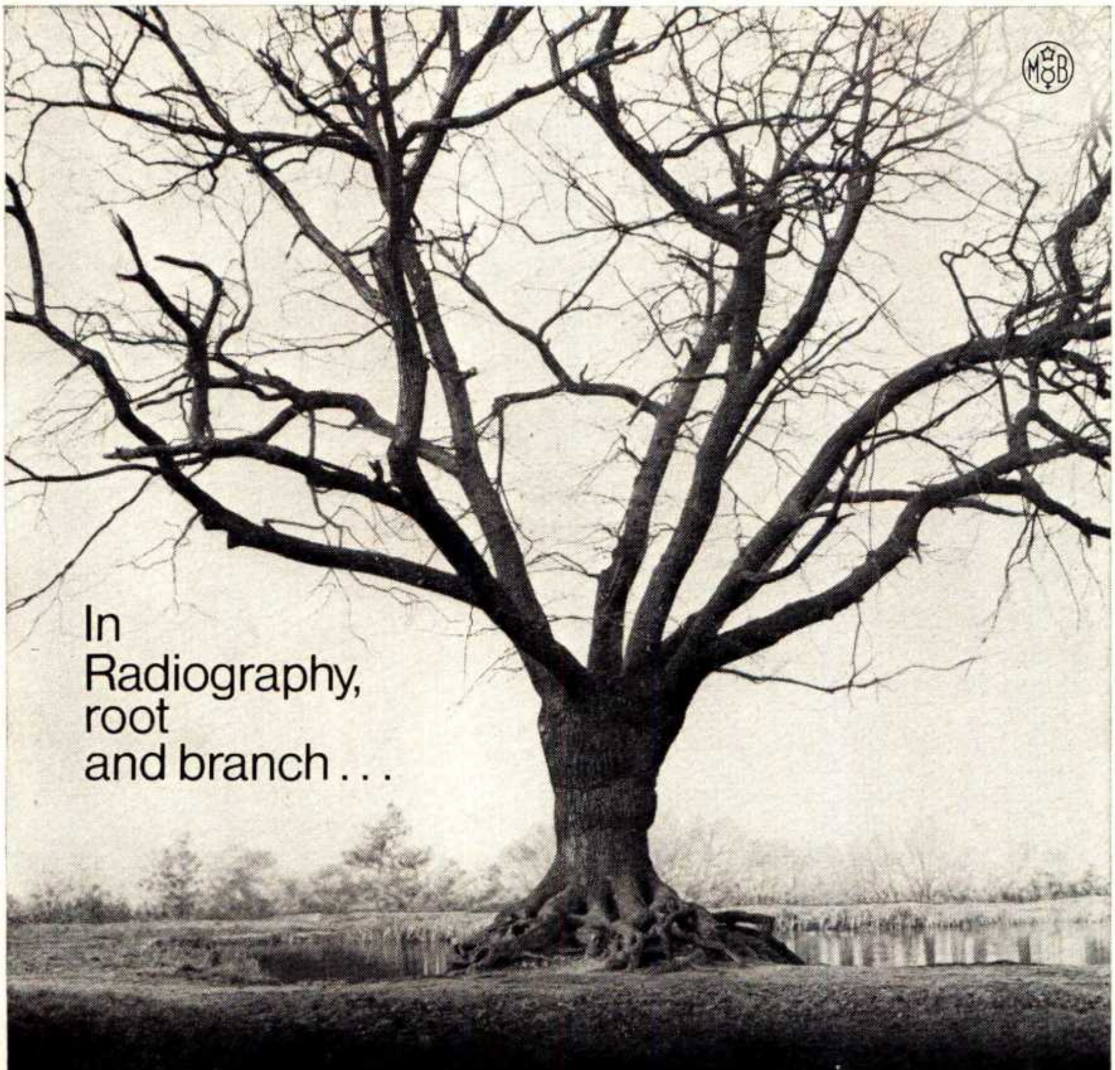

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1. *J clin Path*, (1968), **21**, 202.
2. Symposium: The Synergy of Trimethoprim and Sulphonamides *S Afr med J*, (1970), **44**, Supplement (August) 12.
3. *Brit med J*, (1969), **1**, 541.
4. Leading Article, *Brit med J*, (1969), **1**, 525.
5. Leading Article, *Brit med J*, (1970), **3**, 297.
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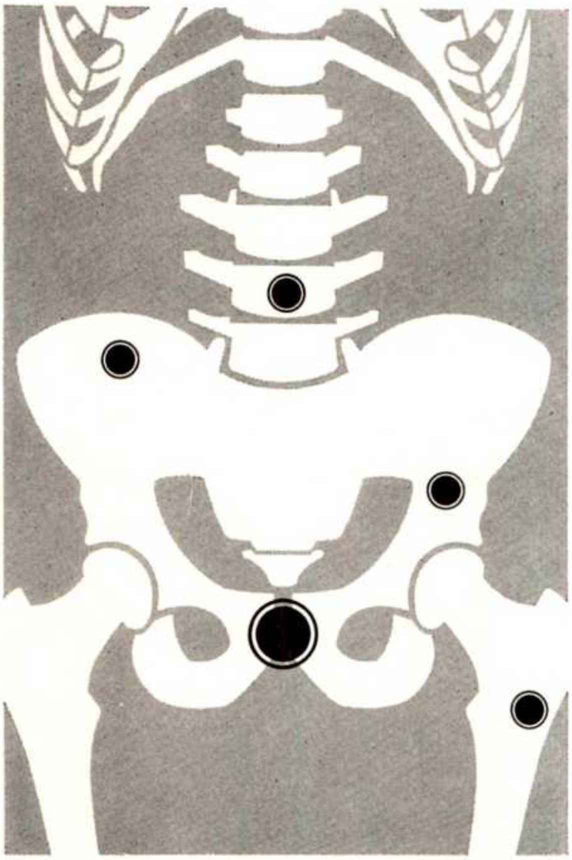

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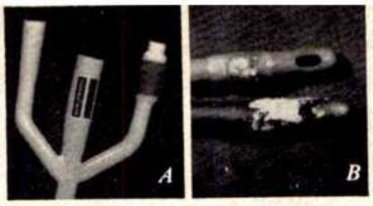

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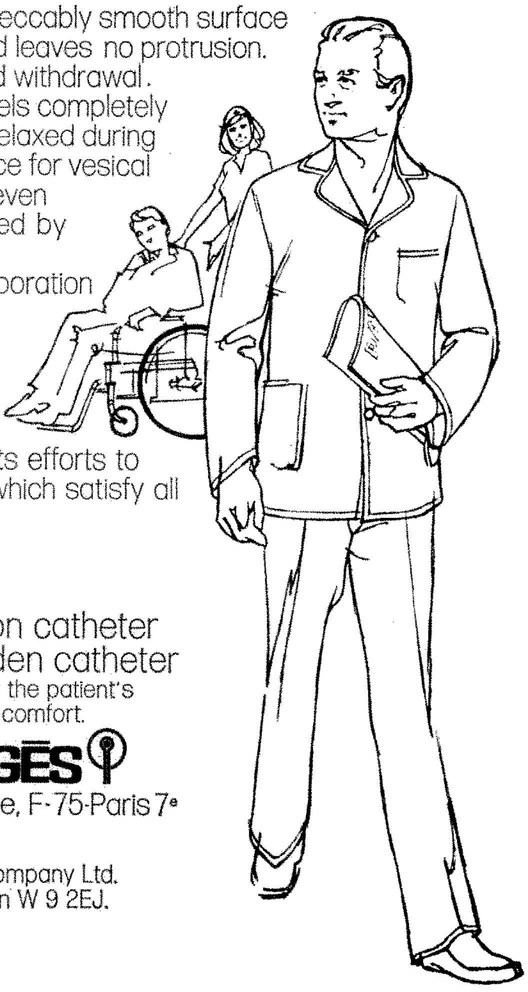

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Brit.J.Urol. 1972 **44,** 105

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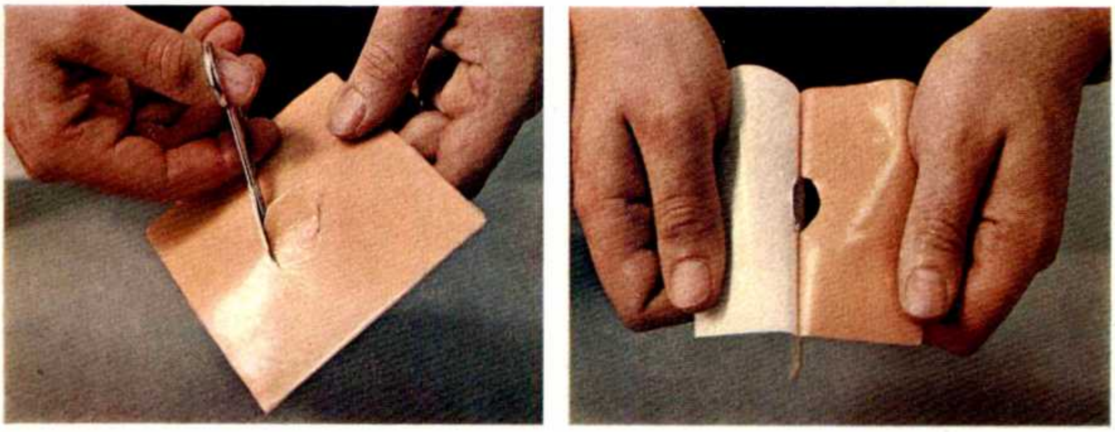

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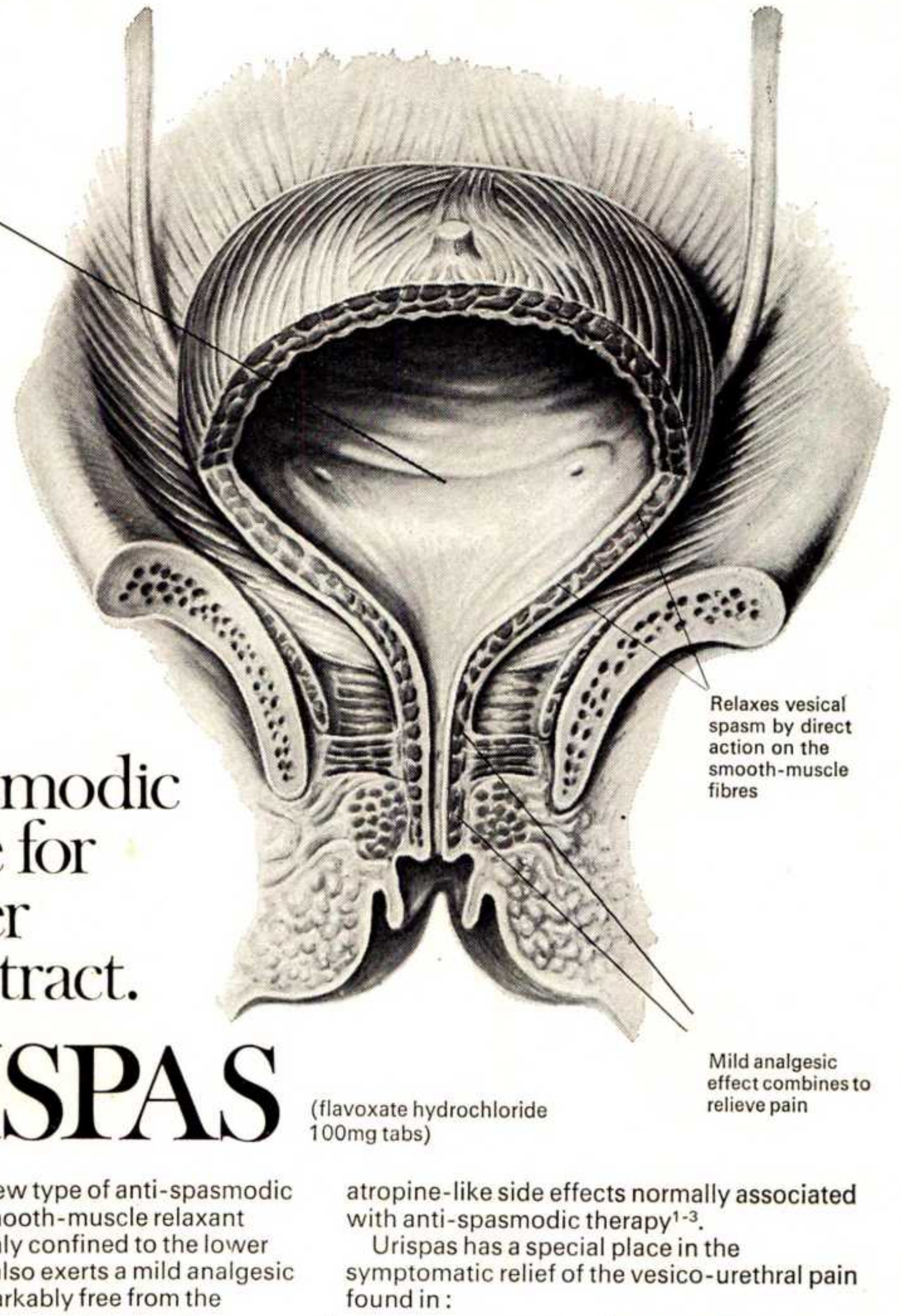
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1. J. Clin. Pharmacol (1970) 10:65
2. J. Urology (1968) 100 (6) 729
3. J. Pharmac. exp. Ther. (1960) 3:354

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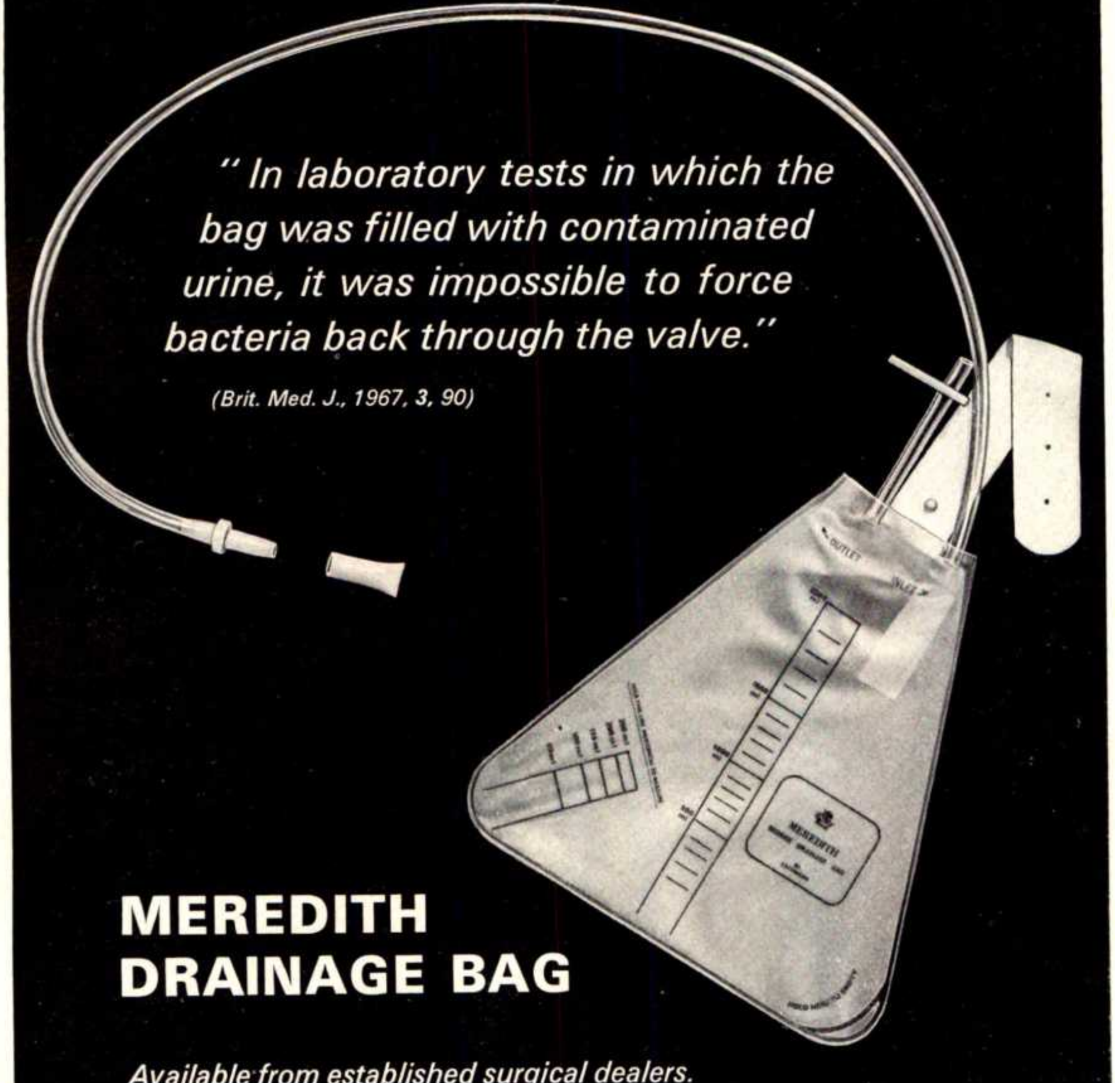

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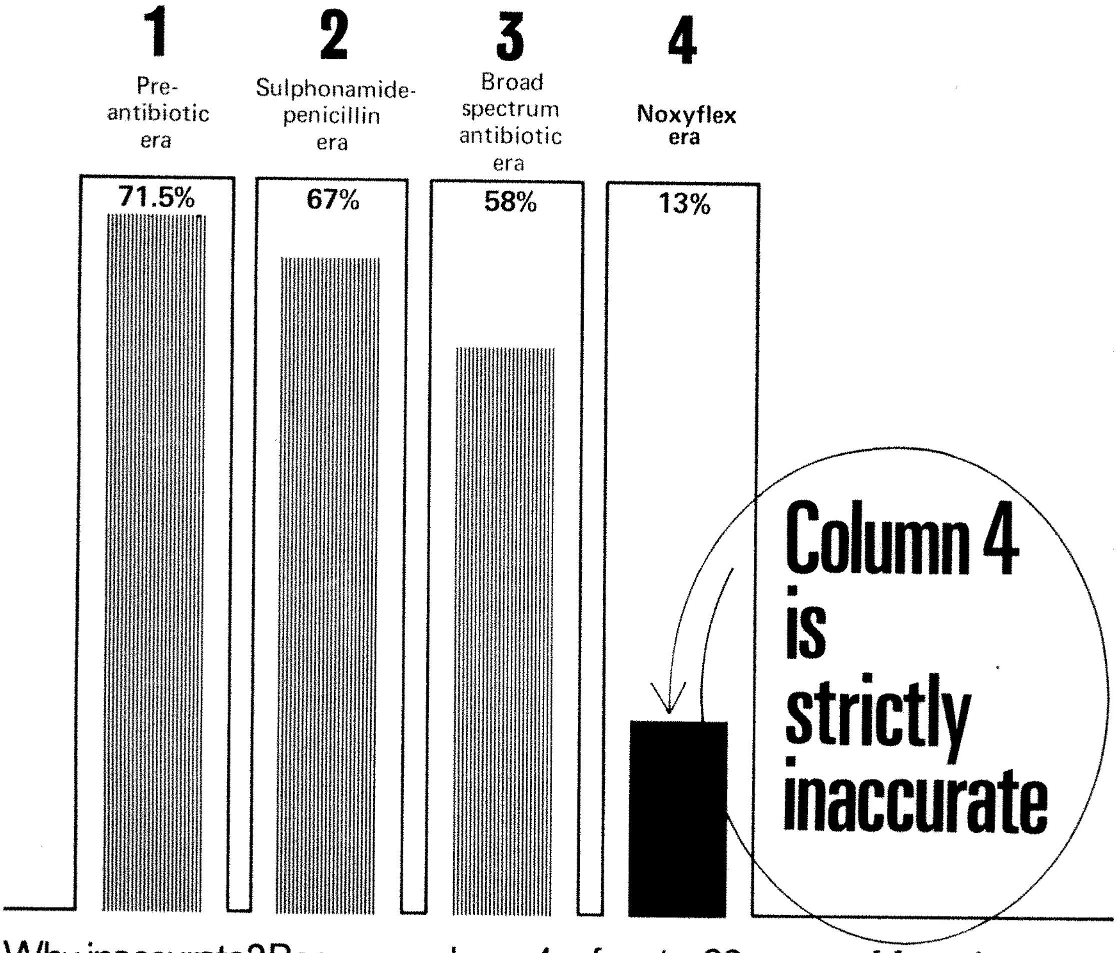

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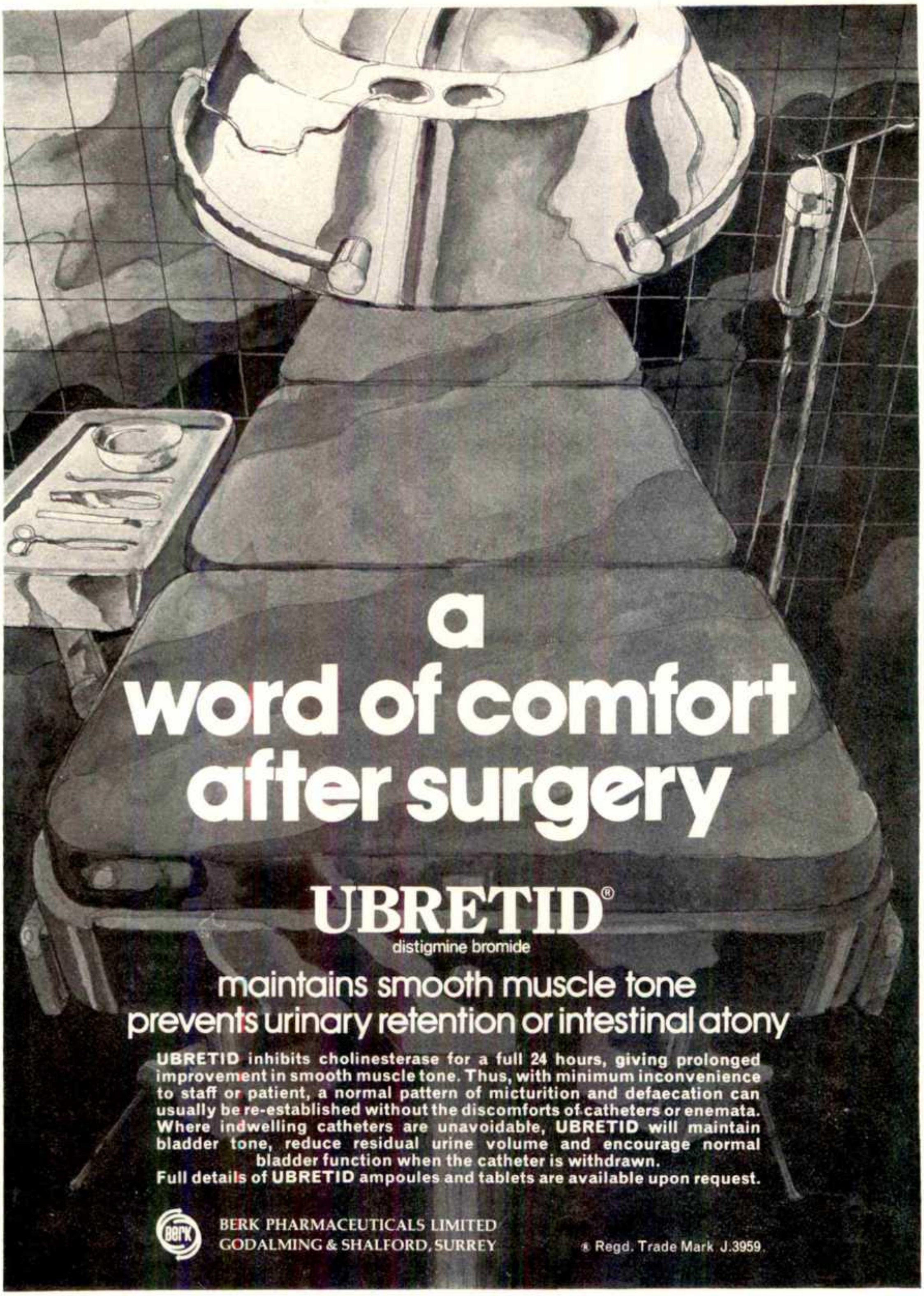

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WHOLE BLOOD, RED CELL AND PLASMA TOTAL AND ULTRAFILTRABLE ZINC LEVELS IN NORMAL SUBJECTS AND PATIENTS WITH CHRONIC RENAL FAILURE WITH AND WITHOUT HÆMODIALYSIS

By G. A. Rose,[1] M.R.C.P., M.R.C.Path. and E. G. Willden, B.Sc.

St Peter's Hospitals and Institute of Urology, London

TRACE elements, of which zinc is one, could be measured in biological fluids only with great difficulty until the introduction of the Atomic Absorption Spectrophotometer in recent years. Plasma zinc, however, can now be measured quite easily by this technique and results in various conditions have already been reported by several independent groups. In these hospitals we were especially interested to know what changes in plasma trace elements might be occurring in patients undergoing regular hæmodialysis, and the following refers to studies in respect of zinc. Since this work was commenced results have been reported from Australia by Blomfield *et al.* (1969), and from Washington D.C., U.S.A., by Halsted and Smith (1970). However, these two groups obtained somewhat different results. Those from Australia showed large rises in plasma zinc on passage through the dialysis coils and this was attributed to the zinc plaster used in the construction of the coils. The American study reported low plasma zinc levels in patients with chronic renal failure without dialysis, with no significant change in plasma zinc after 12 hours of hæmodialysis with Kiil-type dialyser. It was therefore thought of interest to report our own findings with regard to zinc in patients with chronic renal failure whether or not undergoing hæmodialysis.

Methods.—Samples of heparinised blood were obtained from normal volunteers (staff associated with the hospital), patients with chronic renal failure not undergoing dialysis, and from patients with chronic renal failure before, during and after regular twice-weekly hæmodialysis at St Peter's Hospitals, and using Baxter ultra-flow disposable coils in re-circulating single pass artificial kidney machines. In the case of the plasma estimations, the red cells were removed shortly after the samples were obtained. Samples of plasma were also obtained and received by post from patients undergoing regular Kiil hæmodialysis in Newcastle, and Fulham, London. Any visibly hæmolysed specimens were discarded. Although plasma zinc normally shows a diurnal variation (Dawson and Walker, 1969), it was clearly not possible to take all specimens at the same time of day and this aspect has been ignored. Zinc was determined by Perkin-Elmer 290 B Atomic Absorption Spectrophotometer using the de-proteinisation method of Parker *et al.* (1967). This method was applied to plasma, whole blood, plasma ultrafiltrate and bath waters. Each plasma was analysed for urea and creatinine by standard Technicon Auto-Analyser techniques. Hæmoglobin was estimated in the routine hospital pathology laboratory on samples obtained simultaneously with those used for the biochemical tests.

Plasma ultrafiltrates were prepared anaerobically by the method of Rose (1972) using the Amicon filter holder and membrane.

Results.—The zinc levels in whole blood, plasma and plasma ultrafiltrates for normal males and females and for patients with chronic renal failure with and without dialysis on the Baxter ultra-flow system are shown in Table I.

Plasma zinc and creatinine values during a series of dialyses over a 12-week period are shown in Figure 1.

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From the results in Table I, it is possible, using a simple algebraic expression, to calculate the corresponding red cell zinc values, provided that the packed cell volume (PCV) is known. In the case of the samples from the patients it has been assumed that the PCV in each case was proportional to the hæmoglobin value actually measured, and that a PCV of 47 per cent corresponded to a hæmoglobin of 100 per cent. In the case of the normal subjects, hæmoglobin and PCV values were unfortunately not obtained on the same samples and it has therefore been necessary to assume a mean normal PCV of 47 per cent for males and of 41 per cent for females and use these values together with the mean plasma and whole blood zinc levels to calculate the mean red cell values. The red cell zinc values obtained by these various calculations are shown in Table II for normal males and females and patients with renal failure with and without dialysis.

A comparison of results obtained with the Kiil method of hæmodialysis is shown in Table III.

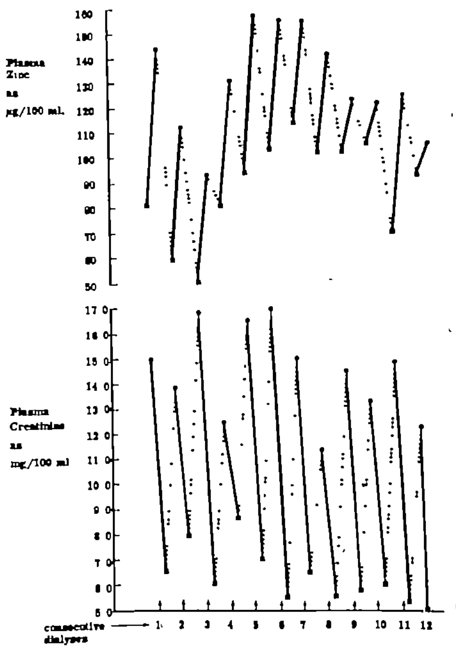

FIG. 1

Pre- and post-dialysis plasma zinc and creatinine levels from a single patient undergoing repeated hæmodialysis using disposable coils over a 12-week period. Continuous lines connect points immediately pre- and post- the same dialysis.

Pre- and post-coil plasma samples were obtained from 26 of the St Peter's dialyses. The mean zinc levels were 97 ± S.D. 31·2 and 130 ± S.D. 71·7 µg./100 ml. respectively. The bath water was made up with 48·3 per cent hard water containing 7µg./100 ml. zinc, 48·3 per cent of soft water containing no zinc and 3·4 per cent of salt concentrate containing 44 µg./100 ml. of zinc. The concentration of zinc in the resultant mix was 7·4 and 23 µg./100 ml. pre-dialysis and post-dialysis respectively (mean of 30 determinations in each case).

DISCUSSION

The normal range reported here for plasma zinc in males is substantially similar to, although slightly lower than, the values reported by Blomfield *et al.* (1969), Davies *et al.* (1968) and by Halsted and Smith (1970). Unlike previous authors, however, we have found that the mean value for normal males is higher than that for normal females. Although these differences are not large, they are statistically significant, and furthermore similar differences have been found in the cases of chronic renal failure not undergoing dialysis. A similar sex difference has also

TABLE I

Zinc in Blood, Plasma, and Plasma U/F. µg./100 ml.

	Normals				Chronic renal failure				Chronic renal failure: Ultra-flow coil								
					No dialysis				Pre-dialysis				Post-dialysis				
	No.	Mean zinc	S.D.	Range	No.[1]	Mean zinc	S.D.	Range	No.[1]	Mean zinc	S.D.	Range	Mean zinc	S D	Range	ΔZn	S.D.
Whole Blood																	
Males	14	585	15·3	560–625	11 (17)	701	72·9	570–830	7 (23)	413	91·4	250–554	538	78·4	413–650	120	60
Females	15	546	18·7	520–580	8 (10)	623	74·8	500–750	6 (20)	357	79·8	260–500	441	102	330–600	84	16·8
Plasma																	
Males	37	85	18·0	50–118	6 (22)	81	11·4	65–100	12 (108)	102	32·4	75–191	135	32·5	100–226	33	9·7
Females . . .	34	75	21·0	43–123	8 (16)	60	14·6	45–90	10 (112)	102	25·5	81–168	137	26·2	105–200	35	7·9
Females (pregnant) . .	4			94–163													
Plasma ultra-filtrate																	
Males . . .	7	50	7·8	41–60	5	60·9	1·8	58–63									
Females	5	55	5·8	40–71	2	51	—	47–55									

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[1] The figure without parenthesis is the number of patients, the figure in parenthesis the number of samples analysed.

been found in the whole-blood zinc levels from patients with chronic renal failure whether or not undergoing dialysis. It is to be noted in this connection that in four normal pregnant females, the plasma zinc levels were raised, although the numbers here are too small to be significant. Thus the sex differences now reported for zinc in normal subjects are similar to those reported by others for copper, *i.e.* higher in males than in females but raised in pregnant females. It might be that hormonal changes alter the protein bound zinc as is known to occur with copper. Thus the plasma ultrafiltrable zinc values now reported are similar in normal males and females.

TABLE II

Calculated Zinc Content in μg./100 ml. of Red Cells

	Number	Mean zinc	S.D.
Normal males	14	1196	60
Normal females	15	1252	58
Renal failure, no dialysis, males	11 (17)	3092	1017
Renal failure, no dialysis, females	8 (10)	2895	536
Renal failure, pre-dialysis, males	7 (23)	3304	709
Renal failure, pre-dialysis, females	6 (20)	2245	808
Renal failure, post-dialysis, males	7 (23)	3458	468
Renal failure, post-dialysis, females	6 (20)	2485	363

TABLE III

Zinc in Plasma of Patients Pre- and Post-Kiil Dialysis

	Newcastle			Fulham		
	Pre-Kiil	Post-Kiil	Rise	Pre-Kiil	Post-Kiil	Rise
No. of patients	5	5	5	19	19	19
Mean plasma zinc	65	89	25	76	95	19
S.D.	7·7	9·3	11·3	15·1	22·7	13·9
Range	54-74	77-104	8-39	56-102	66-136	2·0-60

In chronic renal failure without dialysis, the plasma zinc was found to be slightly reduced, although this reduction was not statistically significant. Definitely reduced plasma zinc levels were reported in uræmic patients not undergoing dialysis by Mansouri, Halsted and Gombos (1970), but their patients were on a protein intake restricted to 20-30 g. per day, whereas patients in this study were not so restricted. On the other hand the whole-blood zinc levels were raised in our patients with chronic renal failure not undergoing dialysis. Since these patients were all anæmic with hæmoglobin levels of about 50 per cent the red cell zinc levels must have been very greatly raised and this is confirmed on calculations of actual values as shown in Table II. Mansouri *et al.* (1970) found slightly raised red cell zinc levels in 4 of their 7 patients not undergoing hæmodialysis, but they appeared uncertain of the significance of this observation. There can be no uncertainty about the interpretation of our results which show a two- to three-fold rise in red cell zinc and this raises questions which we cannot at present answer about how and why such a excess of zinc can have occurred and in what form it is held.

Repeated dialysis completely altered the situation in the patients with chronic renal failure. Thus (Table I) the pre-dialysis plasma zinc levels were raised, but with no difference between males and females, and there was a further rise during dialysis. Pre-dialysis whole-blood zinc levels were low (Table I), with females lower than males, but red cell zinc values are clearly raised (Table II), with the values for males higher than those for females. Dialysis again resulted in further rises in whole blood zinc levels which cannot be explained by changes in hæmoglobin, since the latter were minimal.

Inspection of the Tables and of Figure 1 clearly reveal that dialysis at St Peter's Hospitals was associated with a marked rise in plasma and whole-blood zinc. The source of this zinc cannot be the red cells themselves. Neither could the dialysis fluid have been such a source, firstly because the zinc content in the pre-dialysis bath water was well below that of the normal plasma ultrafiltrable zinc and secondly because the zinc content of the bath water also rose during the dialysis. Since the zinc in plasma taken immediately pre-coil was lower than the corresponding level immediately post-coil it is clear that the source of the zinc must have been in the coils themselves. A similar conclusion was reached by Blomfield *et al.* (1969) in Australia, who suggested that the zinc plaster used in constructing the coils was responsible and recommended that alternative materials should be used. Unfortunately enquiries have so far failed to reveal whether or not the manufacturers have been able to find such alternative materials.

In the case of Kiil dialysis the plasma results were similar from the two centres but quite different from those obtained at the St Peter's Hospitals. Thus the plasma levels pre-dialysis were normal, or even below normal, while the rises during dialysis are much smaller than found at St Peter's Hospitals using the disposable coils. These findings are consistent with the theory that most of the zinc comes from the coils.

It is clearly incorrect to assume that hæmodialysis is the sole cause of zinc retention in chronic renal failure, as shown by the levels in the red cells. Nevertheless we agree with Blomfield *et al.* (1969) that zinc may be dialysed into patients undergoing hæmodialysis. The extent of the zinc retention reported here is however much greater than that found by others. This is because the other groups did not measure red cell zinc in patients undergoing hæmodialysis with disposable coils. Thus Blomfield *et al.* (1969) did not measure red cell zinc while Mansouri *et al.* (1970) only studied Kiil-type dialysis. Blomfield *et al.* (1969) concluded that zinc retention might not be harmful and might even be beneficial, but nevertheless went on to suggest methods of reducing its extent. The most important such measure was the elimination of zinc plaster from the disposable coils, and we reaffirm this suggestion.

SUMMARY

1. Plasma and whole-blood zinc levels have been estimated in patients with chronic renal failure with and without hæmodialysis with disposable coils and with Kiil artificial kidneys.

2. In the patients not undergoing hæmodialysis plasma zinc levels were slightly sub-normal but red cell zinc levels were elevated.

3. In the patients undergoing hæmodialysis with disposable coils, the plasma zinc levels were raised before dialysis and rose even further during dialysis. Similar results were found for red cell zinc levels and the additional zinc must have come from the disposable coils.

4. With Kiil dialysis, the pre-dialysis plasma zinc levels were slightly sub-normal, and during dialysis the levels rose much less than with the disposable coils.

We should like to thank the Institute of Urology (University of London) for the donation of the Atomic Absorption Spectrophotometer equipment, the physicians and nurses of the Renal Dialysis Unit, St Paul's Hospital, Professor H. de Wardener and Professor J. Swinney for sending plasma samples from Fulham and Newcastle respectively.

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British Journal of Urology (1972), **44**, 287-291

COMPOSITION OF URINARY CALCULI BY X-RAY DIFFRACTION

Collected Data from Various Localities

Parts XII-XIV

Northern Ireland, South Africa and Kuwait

By D. JUNE SUTOR, Ph.D. and SUSAN E. WOOLEY

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THE composition of urinary calculi from Northern Ireland, South Africa and Kuwait is presented here as part of our survey of stone composition on a geographical and historical basis. The amount of the different crystalline constituents present was determined by the method described in Part I of this series of papers (Lonsdale *et al.*, 1968*a*) and the results are presented in the usual ways—according to the percentage number of stones in the collection which contain an observable amount of a compound and according to the weighted percentage amount of each compound present, averaged over all the patients in the collection. The stones have also been classified with respect to the number and types of components present. References to other countries in this series mentioned in the text are as follows—Norwich (Lonsdale *et al.*, 1968*a*), Czechoslovakia, Turkey, Thailand, India and Spain (Lonsdale *et al.*, 1968*b*), Leeds (Sutor and Wooley, 1970), Glasgow, Scotland, United States of America and Sudan (Sutor and Wooley, 1971).

XII Northern Ireland.—Through the kindness of Dr M. McGeown of the Belfast City Hospital we received 63 upper urinary tract calculi from Northern Ireland. The stones came from 37 male and 26 female patients aged from 3 to 73 years, average age equalling 44·8 years. The weight range of the samples is 0·005 g.-70 g., the average weight of a stone 3·03 g. and the average weight of stones formed per patient 4·52 g.

The weighted amount of the different compounds and their percentage occurrence are shown in Table I and the percentage number of the different types of stones is listed in Table II.

The major crystalline constituents are calcium oxalate, calcium phosphate and struvite, and, in this respect, the overall composition of the collection is similar to that of other adult upper urinary tract stones from countries other than Israel and those of Central Europe. As in many industrialised areas, the commonest type of stone is the mixed calcium phosphate and calcium oxalate variety comprising here 32 per cent of the total, but in the Northern Ireland collection this variety is closely followed by the mixed calcium phosphate and struvite type, accounting for 29 per cent of the stones. The collection contains more calcium phosphate than any analysed so far. This is only partly a result of the large number of infection stones consisting of calcium phosphate and struvite since calcium phosphate occurs frequently in other varieties and 12 per cent of the collection consists of calculi of the pure compound. In the other areas of Great Britain studied so far, Norwich, Leeds and Glasgow, the amount of calcium phosphate has also exceeded that in the collections of upper urinary tract stones from Turkey, U.S.A., Sudan, Thailand and India, and comparison of the percentage occurrences of this compound shows that stones containing calcium phosphate are usually more prevalent in Britain. The present collection also contains more struvite than other comparable ones, apart from that from Sudan.

In all, the phosphates make up 64 per cent of the total crystalline material; the other constituents are calcium oxalate (34 per cent) and a small amount of cystine. One of the cystine stones is unusual in that the nucleus, interior and surface all contain cystine and struvite, and a small amount of hydroxyapatite is also present in the interior. The sequence of compounds suggests that either cystine can be deposited in infected urine or the infection was transient. No uric acid or urate is present in this series.

As in most collections of upper urinary tract stones, the nucleus was too small to separate accurately from the interior, or the nucleus and interior were homogeneous. Generally though the composition throughout the individual stones is fairly uniform.

XIII South Africa.—The 49 upper urinary tract stones comprising the South African collection were studied through the courtesy of Dr M. Modlin of the Medical School, Cape Town. Their weights range from 0·01 g. to 20 g. The average weight of a stone is 0·63 g. and the average weight of material per patient is 1·15 g. The patients have an unusual sex distribution in that 23 are males and 25 females (the sex of one is unknown). Their ages vary from 16 to 85 years, average value equalling 45·6 years. Ten of them are Cape Coloured and one is a Bantu. Unfortunately, the numbers are not sufficient to compare the composition of stones from the different races.

The amount and frequency of occurrence of crystalline material in the stones and the different types of calculi are shown in Tables III and IV.

As in most collections of upper urinary tract calculi, the amount of oxalate exceeds that of phosphate. Pure oxalate stones are the most common type accounting for 43 per cent of the total number of calculi and 27 per cent of the stones are mixtures of calcium oxalate and calcium phosphate. A similar distribution in the type of stones also occurs in the U.S.A., but there the total amount of oxalate is greater than in the South African collection. Only 6 per cent of the stones consist of just struvite and calcium phosphate, but struvite sometimes with apatite is present in a further 10 per cent. The collection contains a little uric acid, urate and cystine.

The composition of the Bantu stone is not unusual in that it consists of calcium oxalate monohydrate, carbonate-apatite and struvite, but the sequence of compounds is. A large central nucleus of the phosphates is surrounded by a grey interior and surface of calcium oxalate.

The nucleus could only be sampled separately in 9 stones, and in these it is of similar composition to the interior and surface apart from the Bantu calculus and a secondary infection stone consisting of a nucleus of oxalate and outer layers of struvite and apatite.

XIV Kuwait.—Dr S. N. Salem of Sabah Hospital kindly provided us with 65 upper urinary tract calculi from Kuwait. They are very small and their weights range from 0·005 g. to 1·75 g. The average weight of a stone is 0·33 g. and the average weight of stones per patient is 0·39 g. The ratio of male to female patients in this collection (50 : 15) is higher than in any other studied so far. The patients are also younger with an average age of only 32·9 years and an age range of 18-62 years.

The results of the X-ray analysis of the stones are presented in Tables V and VI.

The composition distribution in Kuwait is similar to that in Turkey, India and America. In all these countries a very high proportion of the crystalline material is calcium oxalate and only a small amount is phosphate. The total amount of calcium oxalate present in this series is 76 per cent and that of calcium phosphate and struvite 10 per cent. About half the stones consist of pure calcium oxalate and this, together with the small number of infection stones (those containing struvite often with apatite), account for the low average weight.

The most common type of stone after the pure oxalate variety is that composed of a mixture of calcium oxalate and calcium phosphate. Such stones are frequently the most important ones in industrialised countries but in Kuwait they account for only 16½ per cent of the calculi.

In Central Europe and Israel uric acid can be an important constituent of kidney stones. The collections we received from Czechoslovakia and Spain contain 24 per cent and 21 per cent of this compound, respectively. Uric acid is present in 20 per cent of the stones from Kuwait and accounts for 12 per cent of the crystalline material. The latter value is intermediate between those for Czechoslovakia and Spain and 5 per cent for the Turkish collection, the highest figure for uric acid in our other collections of upper urinary tract calculi.

Although the overall composition in Kuwait is similar to that in industrialised countries, 4½ per cent of the stones are composed of a mixture of calcium oxalate and ammonium acid urate. This combination of compounds is typical of children's bladder stones from technically developing countries and old museum collections but is rarely found in adult upper urinary tract calculi from industrialised countries and communities (Sutor, 1972).

Again the nuclei of the stones were usually homogeneous with the interiors.

SUMMARY

As part of a world survey of stone composition the crystalline constituents present in collections of upper urinary tract calculi from Northern Ireland, South Africa and Kuwait have been determined by the X-ray powder method. The Northern Ireland stones contain more calcium phosphate than any comparable collection studied so far. Increased amounts of this compound have also been found in other areas of Great Britain and are only partly a result of the number of infection stones consisting of calcium phosphate and struvite. The major constituents of the South African collection are oxalate and phosphate as in most collections of upper urinary tract calculi, but the amount of uric acid (12 per cent) is greater than that found in any collection of such stones from countries outside Central Europe and Israel. The collection from Kuwait is similar to those from America, India and Turkey, all of which contain a very large amount of calcium oxalate. Some of the stones from Kuwait consist of a mixture of calcium oxalate and ammonium acid urate, a combination of compounds commonly found in endemic children's bladder stones from certain areas of technically-developing countries but not usually encountered in upper urinary tract stones from industrialised areas.

We thank the Medical Research Council and Nuffield Foundation for financial assistance.

TABLE I

Composition of the Northern Ireland Stones

No. of stones	C1	C2	D	F1	F2	F3	F4	F5	G2	X
				(*a*) Percentage occurrence of components						
63	49	44	3	49	43	3	13	3	38	1
				(*b*) Weighted percentage composition						
63	18	16	2	26	17	1	3	1	16	>0

Key for all Tables—A1 = anhydrous uric acid, A2 = uric acid dihydrate, B = ammonium acid urate, C1 = calcium oxalate monohydrate, C2 = calcium oxalate dihydrate, D = *l*-cystine, F1 = carbonate-apatite, F2 = hydroxyapatite, F3 = brushite, F4 = whitlockite, F5 = octacalcium phosphate, G2 = struvite, X = unidentified material, C = C1 and/or C2, F = any combination of F1, F2, F3, F4 and F5 etc.

TABLE II

Percentage Number of the Northern Ireland Stones classified according to Compounds present

C1	1½	F	1½
D	1½	C+F	32
F1	3	C+G2	1½
F2	1½	F+G2	29
G2	1½	C+F+G2	5
C1+C2	14	D+F+G2	1½
F1+F2	6		

Key as for Table I

TABLE III

Composition of the South African Stones

No. of stones	A1	A2	B	C1	C2	D	F1	F2	F4	F5	G2
(*a*) Percentage occurrence of components											
49	8	2	10	73	55	2	33	16	2	2	16
(*b*) Weighted percentage composition											
49	3	1	1	41	23	2	14	7	<0	1	7

Key as for Table I

TABLE IV

Percentage Number of the South African Stones classified according to Compounds present

C1	14	A+C	2
C2	6	C+F	27
D	2	F+G2	6
F1	2	A+B+C	2
F2	2	C+F+G2	6
C1+C2	23	B+C+F+G2	4
A +B	4		

Key as for Table I

TABLE V

Composition of Stones from Kuwait

No. of stones	A1	A2	B	C1	C2	F1	F2	G2
(*a*) Percentage occurrence of components								
65	19	7	7	84	69	7	19	10
(*b*) Weighted percentage occurrence								
65	11	1	2	44	32	2	3	5

Key as for Table I

TABLE VI

Percentage Number of the Stones from Kuwait classified according to Components present

A1	3	C1+C2	43
C1	6	C+F	16½
G2	1½	C+G2	1½
A1+A2	3	F+G2	4½
A+B	3	A+C+F	3
A+C	7½	C+F+G2	3
B+C	4½		

Key as for Table I

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British Journal of Urology (1972), 44, 292-295

THE RESULTS OF CONSERVATIVE SURGERY FOR STONE[1]

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PREVIOUS studies have suggested that stone formation is a disorder with a high recurrence rate, which frequently affects both renal tracts and which may recur after long periods of freedom from the disease. In this paper the term " conservative " surgery has been considered to include transurethral techniques such as chemical dissolution of calculi, ureteric meatotomy and ureteric extraction as well as the lithotomy operations on the kidney and ureter; partial nephrectomy and nephrectomy have been excluded. The incidence of late recurrence of stone following lithotomy operations on the upper renal tract however is described and discussed.

Transurethral Surgery

1. *Stone dissolution.*—This method has been recommended by some Continental surgeons (Aboulker, *et al.*, 1966). Residual phosphatic renal stones can be effectively treated by lavage with acid solutions over 8 to 20 days when a nephrostomy tube has been left in place following pyelolithotomy.

In other cases, a double-lumen ureteric catheter with an attached guide wire may be passed at cystoscopy and its tip placed in proximity to the stone under X-ray control. Treatment of oxalic calculi is attempted only if the urine is already infected as the risk of failure is high and does not justify the possibility of introducing infection. In these instances chelating solutions may be more effective. Even with antibiotic cover there is risk of ascending infection and those who have used this technique recommend that it should be employed only when the patient is debilitated and unfit for anæsthesia. Introduction of infection, the risk of septicæmia and loss of renal function have been the major complications of this procedure and it has not been widely accepted.

2. *Ureteric Meatotomy.*—With this established procedure for the relief of stone impacted at the ureteric orifice, the latter may be cut with the meatotome or scooped out with the resectoscope loop, removing œdematous mucosa and stone together. Whichever method is used there is a risk of vesico-ureteric reflux and this may assume greater significance in the presence of urinary tract infection, or may be responsible for persistence of infection should this arise in later years.

3. *Ureteric Extraction.*—Councill (1945), in a review of 504 cases in which the Councill stone extractor and dilator was used, successfully removed calculi in 85 per cent of cases in which he was able to pass the extractor beyond the stone. In the Urology Department at Leeds the success rate is nearer 25 per cent but here an expectant policy is followed with many small calculi; it is impossible to assess what proportion of stones removed by ureteric extraction would have passed spontaneously if left to do so. The use of image intensification radiological methods may increase the success rate for manipulative removal of ureteric calculi.

Apart from minor troubles of tissue bruising and bleeding, we have encountered 3 main problems. On 1 occasion the ureteric wall was perforated by the ureteric extractor and surgical exploration was required to remove both it and the stone; this is more likely to happen if the stone is impacted in the ureter and there is surrounding periureteric inflammation. Secondly, in 2 instances the stone was caught in the extractor and pulled to the ureteric orifice but could not be delivered through the orifice itself; in these circumstances the sheath of the extractor was removed and the patient returned to the ward with the wire extractor still in the ureter. Overnight, both stone and extractor passed into the bladder. Lastly, on 1 occasion the ureteric wall was caught in the extractor leading to avulsion of the lower ureter and subsequently to nephrectomy, as surgical repair was not considered possible.

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[1] Read at the Twenty-seventh Annual Meeting of the British Association of Urological Surgeons in London, June 1971.

These complications can be avoided if the following contra-indications for the manipulative treatment of ureteric calculi are followed: (1) When the stone is known to have been present for some time and considerable peri-ureteritis may have developed. (2) When the stone is in the middle or upper third of the ureter. (3) When hydronephrosis and hydro-ureter are present. (4) When there have been previous unsuccessful attempts to remove the stone.

3. *Recurrence Following Lithotomy Operations.*—A long-term follow-up of 538 patients who had experienced 1948 " clinical episodes " of stone was described by Williams (1963). In most (62 per cent) of these patients the clinical incident was the spontaneous passage of a calculus; while in others it was a stone identified on X-ray which had neither passed spontaneously nor had been removed surgically for a variety of other reasons—usually the poor general health of the patient or the fact that the stone was producing no symptoms. A further 28 per cent of the clinical incidents was accounted for by 554 operations for removal of stone. While some of these patients have since been lost to follow-up or have died, many have continued to attend for regular X-ray and are available for continued study. Operation cases included in the present study were taken from the 554 with operations in that series; patients who had had a nephrectomy or partial nephrectomy were excluded as were those with residual ipsilateral calculi—usually staghorn calculi or other large stones, fragments of which had been left in the kidney.

All operations selected for the present analysis had had calcium-containing stones and immediately after operation were known to be radiologically free from calculi in the ipsilateral kidney; they numbered 257 operations. From these it was possible to study the true ipsilateral recurrence rate and for the purpose of this study contralateral recurrence has been ignored. The operation was classified as pyelolithotomy when surgery was limited to an incision in the renal pelvis (any operation that also involved incision of the renal parenchyma was classified as nephrolithotomy).

TABLE I

Conservative Operations for Stone

	No. of operations	No. of patients	Sex	
Nephrolithotomy	87	75	Male	49
			Female	26
Pyelolithotomy	75	67	Male	38
			Female	29
Ureterolithotomy	95	88	Male	68
			Female	20
	257			

The total of 257 operations available for follow-up is distributed as shown on Table I. There is a high incidence of nephrolithotomy due to the definition that any operation involving incision in the renal parenchyma would be thus classified. Pyelolithotomy is shown to be the commonest operation in females and the preponderance of uretero-lithotomy in males is also seen.

When the lithotomy operations are studied in successive 5-year periods (Table II), the incidence of recurrence is found to rise progressively with each period. For those operations in which a 20-year follow-up is available, the incidence of recurrence reaches 80 per cent.

TABLE II

True Ipsilateral Recurrence Following Lithotomy Operations

Nephrolithotomy—87 operations					
Duration of follow-up (yrs.)	1	5	10	15	20
No. available for study	87	84	77	69	59
Recurrence %	6	17	24	53	78
Pyelolithotomy—75 operations					
Duration of follow-up (yrs.)	1	5	10	15	20
No. available for study	75	71	60	47	39
Recurrence %	6	8	37	65	80
Ureterolithotomy—95 operations					
Duration of follow-up (yrs.)	1	5	10	15	20
No. available for study	95	86	69	51	44
Recurrence %	6	21	35	51	70

DISCUSSION

Sutherland (1954) drew attention to the high incidence of recurrence following lithotomy operations when followed up for an average of 8 years. Williams (1963, 1968) showed a high incidence of recurrence following both the spontaneous passage and operation for the removal of stone in a large series of patients available for prolonged follow-up. These results contradicted the report of Garvey and Boyce (1956) who stated that about 85 per cent of patients have a single episode if a small stone is passed spontaneously and also that of Baker and Connelly (1956) who found that 90 per cent of their patients with 1 renal calculus never developed another. Blacklock (1968) in a careful study of personnel in the Royal Navy, found recurrence rates similar to those quoted by Williams (1963); he also related the incidence of urolithiasis to occupation.

The present study was limited to ipsilateral recurrence of stone in circumstances when that side of the urinary tract was known to be free from stone following operation and thus afforded an opportunity for careful study of recurrence rates. No difference in recurrence rate was found among the operations of nephrolithotomy, pyelolithotomy and ureterolithotomy so this study does not support the results of Sutherland (1954) who found a higher incidence of recurrence following nephrolithotomy operations and suggested that this was due to damage to the renal parenchyma at that operation.

The high incidence of recurrence following operative surgery would suggest that conservative measures for removal of stone should be employed whenever possible. Nephrectomy should be avoided apart from instances of gross renal damage and recurrent infection. If contralateral recurrence of stone had been included, the overall recurrence rate would be higher still.

While it is recommended that all patients with stone formation should attend regularly for follow-up and radiological investigation, it is appreciated that recurrence may be delayed for many years and that prolonged follow-up on a large number of patients may not be possible within the work-load of a busy urological department.

In summary, nearly 80 per cent of patients who undergo lithotomy operations develop an ipsilateral recurrence, and this recurrence may occur after a long interval without stone formation.

I thank my colleagues, Mr P. B. Clark and Mr P. H. Smith for their permission to study the patients under their care.

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XANTHOGRANULOMATOUS PYELONEPHRITIS

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In the 55 years since the initial description of its pathologic features by Schlagenhaufer (1916), xanthogranulomatous pyelonephritis has gradually gained wider recognition and received no less than 7 names, each emphasising one of more of its characteristics (Anhalt *et al.*, 1971). Several recent comprehensive reviews adequately describe some of the clinicopathologic features of this entity, and each contains a few additional case reports (Noyes and Palubinskas, 1969; Tonelli and Giannotti, 1969; Anhalt *et al.*, 1971).

A critical evaluation of 18 cases of xanthogranulomatous pyelonephritis treated at the Mayo Clinic in the past 53 years (1918 through 1971), emphasising its multiple facets and suggesting a classification of this great imitator, is the subject of our report.

Materials and Methods.—Among 3,000 consecutive nephrectomies and open biopsies performed for various reasons, with subsequent findings of chronic pyelonephritis: in 18, features of xanthogranulomatous pyelonephritis were found; 9 of these cases were previously reported (Selzer *et al.*, 1957; Vermillion *et al.*, 1970). A summary of data pertaining to further evaluation and follow-up of the reported case and to additional new cases is presented in chronologic order in Table I.

OBSERVATIONS

Clinical Features.—Both sexes were equally affected. The age range was from 15 to 70 years (mean, 47·5 years).

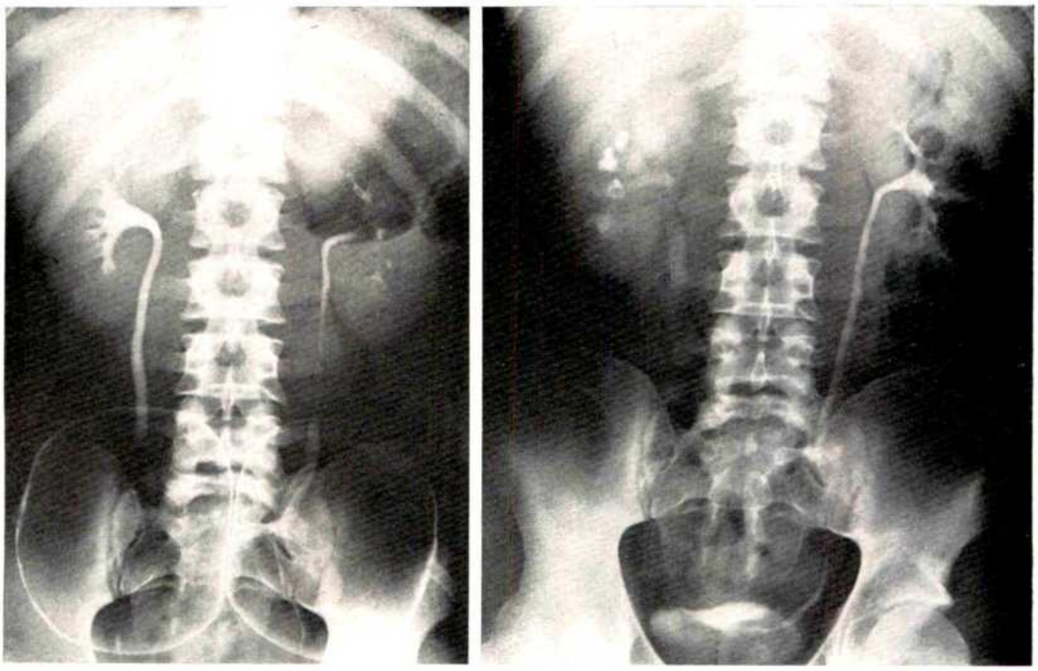
All but 2 patients, who presented only with flank pain, had multiple symptoms and physical findings including renal pain or colic in 15, recurrent low-grade fever in 8, chills in 7, malaise, anorexia and weight loss in 7, hæmaturia in 3, cystitis in 2, flank mass in 2, and draining flank sinus in 1. Two other patients had had flank sinuses which had ceased to drain before their evaluation here. The duration of symptoms and findings ranged from 2 weeks to 5 years (mean, 10 months).

The history was relevant in 12 of the 18 patients. As a result of mis-diagnosis (Fig. 1) a young man (case 14) had received isonicotinic acid hydrazide and *p*-aminosalicylic acid for suspected genito-urinary tuberculosis.

Physical examination was negative in 1 patient but disclosed a flank mass in 14, hepatomegaly in 6, and hypertension in 2 patients. Other findings included draining flank sinus, goiter, generalised acne with pyoderma, and bilateral nephrostomies, each in 1 patient.

Bacteriology.—Cultures of urine pre-operatively and of renal tissue post-operatively were obtained in 15 patients. No urosepsis was found in 7 patients; the remaining 8 had *E. coli*, *Pseudomonas*, or *Proteus* bacilluria (mixed infection in 1). Cultures of renal tissue were positive in all patients; the offending pathogens were *Escherichia coli*, *Proteus*, *Pseudomonas*, *Aerobacter*, *Staphylococcus aureus*, *Klebsiella*, and *Streptococcus faecalis* in that order (mixed infections in 2). Extensive tests for tuberculosis, brucellosis, and mycotic infections all were negative in the same 15 patients.

Hepatic Dysfunction.—Seven patients manifested some of a combination of biochemical abnormalities commonly known as " nephrogenic hepatic dysfunction " which is usually characterised by increases in serum alkaline phosphatase, glutamic-oxaloacetic transaminase, α_2-globulin



A FIG. 1 B

Fig. 1 (case 14).—Excretory urograms. A, at time of cholecystitis with abscess, showing bilaterally normal upper urinary tracts. B, At 2 years later, showing right renal changes compatible with renal tuberculosis; subsequent nephrectomy disclosed xanthogranulomatous pyelonephritis confined to kidney. Left side is normal.

Fig. 2 (case 11).—Nephrotomogram, showing cystic lesion with punctate calcification at site of previous lower left heminephrectomy for calculi (*arrows*); subsequent nephrectomy disclosed nephric and perinephric xanthogranulomatous pyelonephritis. Right side is normal.

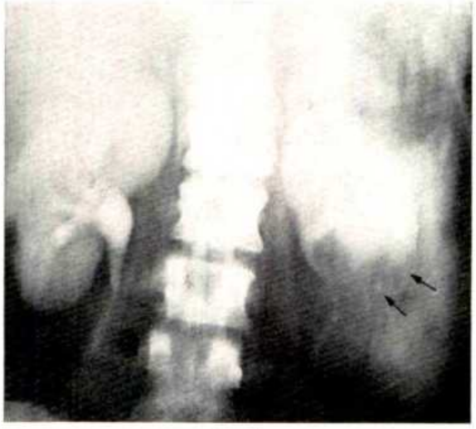


FIG. 2

(and occasionally α_1-globulin), and sulfobromophthalein (BSP) retention with hyperbilirubinæmia and hypoprothrombinæmia (increased prothrombin time) (Table II). Hepatomegaly, another feature of the syndrome, was present in 4 members of this group; liver biopsy in one (case 17) showed non-specific focal hepatitis.

Rœntgenographic and Pre-operative Diagnosis.—Urographic studies in all patients, supplemented by nephrotomography in 4, renal angiography plus inferior venacavography in 1, and radio-iodohippurate renal scanning in 1, disclosed a renal mass lesion in 12 (with calcification (Fig. 2) in 3), a functionless kidney in 3, and a hydronephrotic kidney in 3. The contralateral kidney was normal (1 had a small simple cyst) in 17 and poorly functioning in the 1 patient with

TABLE I

Summary of Data in 18 Cases of Xanthogranulomatous Pyelonephritis (XGP)

Case	Sex; age (yr.)	Symptoms	History	Physical findings	Cultures[1]	Hepatic dysfunction	Urographic findings	Pre-operative diagnosis	Operative procedure and pathology	Follow-up
1	M 50	Colic and ache, L. flank; 2 wk.		Tender fixed mass, L. flank hepatomegaly		No	Mass, upper pole, L. kidney	Renal tumour, L.	Exploration and biopsy, L. renal mass; *Nephric and perinephric XGP*	Alive, 6 mth.
2	F 50	Colic, L. flank; weakness; loss, 40 lb.; 6 mth.		Tender mass, L. flank; hepatomegaly		No	Functionless L. kidney with staghorn calculus	Calculus, pyonephrosis, L.	Nephrectomy, L; *Nephric and perinephric XGP*	Alive, 10 yr.
3	F 58	Pain, L. abdomen; anorexia; loss, 10 lb.; 1 mth.	Hypertension, 2 yr.	Normotension; atrial fibrillation; tender mass, L. flank		No	Mass, lower pole, L. kidney	Renal tumour, L.	Nephrectomy,L.; *Nephric and perinephric XGP*	Lost
4	M 30	Colic, L. flank; chills and fever daily (103°F); 2 mth.		Tender, L. flank	Urine: neg. Kidney: *S. aureus*	No	Deformity, upper pole, calyces, L. kidney	Renal carbuncle, L.	Nephrectomy, L.; *Nephric and perinephric XGP*	Alive, 11 yr.
5	F 60	Colic, L. flank; chills and fever; hæmaturia; cystitis; 1 mth.	Questionable density, lower pole, L. kidney, 15 yr. ago	Tender, L. flank	Urine and kidney: *E. coli, Pseudomonas*	No	Mass, lower pole, L. kidney with calcification	Renal tumour or TB, L.	Exploration and biopsy, L. renal mass; *Nephric and perinephric XGP*	Died, 15 yr. (cerebral hæmorrhage)
6	M 48	Pain, L. flank, and fever, 2 yr.; draining sinus, L. flank, 10 days	Incision and drainage, mass, L. flank, 1 mth. ago (elsewhere)	Draining sinus and fluctuant mass, L. flank	Urine: *E. coli* Sinus: *E. coli*	No	Mass, mid-portion and lower pole, L. kidney	Draining perinephric abscess, L.	Incision, drainage, and biopsy, sinus, L. flank; nephrectomy, L., 3 mth. later; *Nephric and perinephric XGP*	Died, 18 yr. (colonic carcinoma)
7	M 70	Pain, L. flank; 1 mth.	Recurrent L. ureteral colic: L. ureteral lithotomy wound (1 yr. ago) drained for 8 mth.		Urine: *E. coli* Kidney: *Aerobacter*	No	Functionless L. kidney	Functionless L. kidney with urosepsis	Nephrectomy, L.; *Nephric XGP*	Died, 10 yr. (gastric carcinoma)

8	M	60	Pain and mass, L. flank; fever daily (101°F.); 2 mth.	Cystolithotomy with prostatectomy; heminephrectomy, lower pole, R. duplex kidney for calculi, 6 yr. ago	Large, tender mass, L. flank	Urine: neg. Kidney: *S. aureus*, *Pseudomonas*, and *Strept. faecalis*	No	Mass adjacent to functionless stone-bearing lower segment, L. duplex kidney; normal upper segments bilaterally	Perinephric abscess, L.	Incision and drainage, abscess L. flank; hemi-nephrectomy, lower segment, L.; drainage, retroperitoneal abscess, L.; *Nephric* and *perinephric XGP*	Died, 12 yr. (chronic renal failure, hypertension, obstructive lung disease)
9	M	65	Fatigue; night sweats; 1 mth.	Transurethral prostatic and later vesical neck resection; urosepsis (*E. coli*) 2 yr. ago	Goiter; mild hypertension (118 112 mm. Hg)	Urine: neg. Kidney: *Proteus*	Yes	Mass, lateral aspect, L. kidney	Renal tumour, L.	Nephrectomy, L.; *Nephric and perinephric XGP*	Alive, 4 yr. (primary myxœdema)
10	F	40	Pain, both flanks; chills and fever; hæmaturia; 4 yr.		Tender flanks; hepatomegaly	Urine: *Proteus* Kidney: *Proteus and Aerobacter*	Yes	Mass, multi-locular, 7 × 10 cm., upper pole, stone lateral aspect, L. kidney; normal R. kidney with small stone, lower pole	Renal tumour, L.	Nephrectomy, L.; splenectomy for adhesions; *Nephric and perinephric XGP*	Alive, 6 mth.
11	F	29	Pain, L. flank; chills and fever; 3 wk.	Heminephrectomy, lower pole, L. (infected lithiasis 1 yr. ago; draining wound sinus for 6 mth.	Mass, non-tender beneath mid-portion of flank incision, L.	Urine: *E. coli* Kidney: *E. coli*	No	Multicystic mass with punctate calcification attached to normal upper segment, L.	Postop. abscess, L. flank	Nephrectomy, L.; *Nephric and perinephric XGP*	Lost
12	F	52	Abdominal mass, R.; anorexia; fever (100°F.); 1 yr.	Laparotomy (elsewhere), 1 yr. ago (diag.: retro-peritoneal fibrosis)	Mass, hard, fixed, 15 × 15 × 10 cm. R. abdomen	Urine: *E. coli* Kidney: *Proteus*	Yes	Huge mass with calcification, lower ½ R. kidney, with much displacement of right colon and inferior vena cava	Invasive renal tumour, R. (angiogram not characteristic	Exploration, nephrectomy, and removal retroperitoneal mass, R.; *Nephric, perinephric, and paranephric XGP*	Lost
13	M	56	Pain, R. flank; 1 yr.	Multiple bilateral renal oper., obstructive and infected renal stones, 34 yr.; nephrostomies, R., 15 yr., and L.,1 3 yr.	Bilateral nephrostomies; tender R. flank	Urine: *Pseudomonas* Kidney: *Proteus*	Yes	Poor function; calculi bilaterally, R. > L.; ureteropelvic obst., R.	Calculous pyonephrosis with poor function and useless nephrostomy tube, R.	Nephrectomy, R.; *Nephric and perinephric XGP*	Alive, 1 yr. (renal insufficiency)

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[1] Urine cultures were pre-operative; kidney cultures, at operation.

[*continued overleaf*

TABLE I—*continued*

Case	Sex; age (yr.)	Symptoms	History	Physical findings	Cultures[1]	Hepatic dysfunction	Urographic findings	Pre-operative diagnosis	Operative procedure and pathology	Follow-up
14	M 19	Anorexia; malaise; chills; hæmaturia; cystitis; 3 mth.	Cholecystectomy and drainage of abscess 2 yr. ago; anti-TB treatment (INH and PAS) 5 days	Acne with pyoderma: hepatomegaly treatment	Urine: neg. Kidney: group IVD gram-neg. bacillus	Yes	Hydronephrosis with upper pole calyceal blunting, R.	Subhepatic abscess and renal TB, R.	Laparotomy and nephrectomy, R. (no subhepatic abscess); *Nephric XGP*	Alive, 1 yr. (no anti-TB treatment)
15	F 15	Pain, R. flank; urosepsis; 5 yr.		Tender R. flank	Urine: *E. coli* Kidney: *E. coli*	No	Mass, mid-portion, R. kidney	Renal abscess, R.	Exploration, excision and drainage calyceal abscess, R. kidney; *Nephric XGP*	Alive, 6 mth.
16	F 57	Pain, R. flank; malaise; chills; 2 wk.	Repair, ureteropelvic obst., 5 yr. ago; chronic pyelohephritis with poor function, R., diagnosed 4 yr. ago	Tender R. flank	Urine: neg. Kidney: *E. coli*	No	Markedly hydronephrotic, functionless R. kidney; normal L. kidney with small cortical cyst	Pyonephrosis, R.	Nephrectomy, R.; *Nephric XGP*	Alive, 3 mth.
17	F 29	Pain, R. flank chills; 2 wk.	Insignificant ureteropelvic obst. diagnosed 4 yr. ago; hypertension (normal renal angiogram) and recurrent urosepsis 10 yr.	Tender R. flank; hepatomegaly; hypertension (200/110 mm. Hg)	Urine: neg. Kidney: *Klebsiella*	Yes	Poorly functioning R. kidney with ureteropelvic obst. and stone, lower pole	Hydronephrotic R. kidney with ureteropelvic obst. (renal scan showed " cold " area, upper pole, R. kidney	Nephrectomy, R.; liver biopsy (non-specific focal hepatitis); *Nephric and perinephric XGP*	Well, 2 mth.
18	M 67	Fever (102°F.); loss 20 lb.; 6 mth.	L. renal stone passed, 5 mth. ago; cholecystectomy and transrectal biopsy and fulguration, rectal polyp (grade I, adenocarcinoma) 1 mth. ago	Hepatomegaly	Urine: neg. Kidney: *E. coli*	Yes	Mass, upper pole L. kidney; normal R. with small stone, mid-portion	Renal tumour, L.	Nephrectomy, L.; *Nephric and perinephric XGP*	Alive, 2 mth. postop. (primary hyperparathyroidism)

[1] Urine cultures were pre-operative; kidney cultures, at operation.

TABLE II

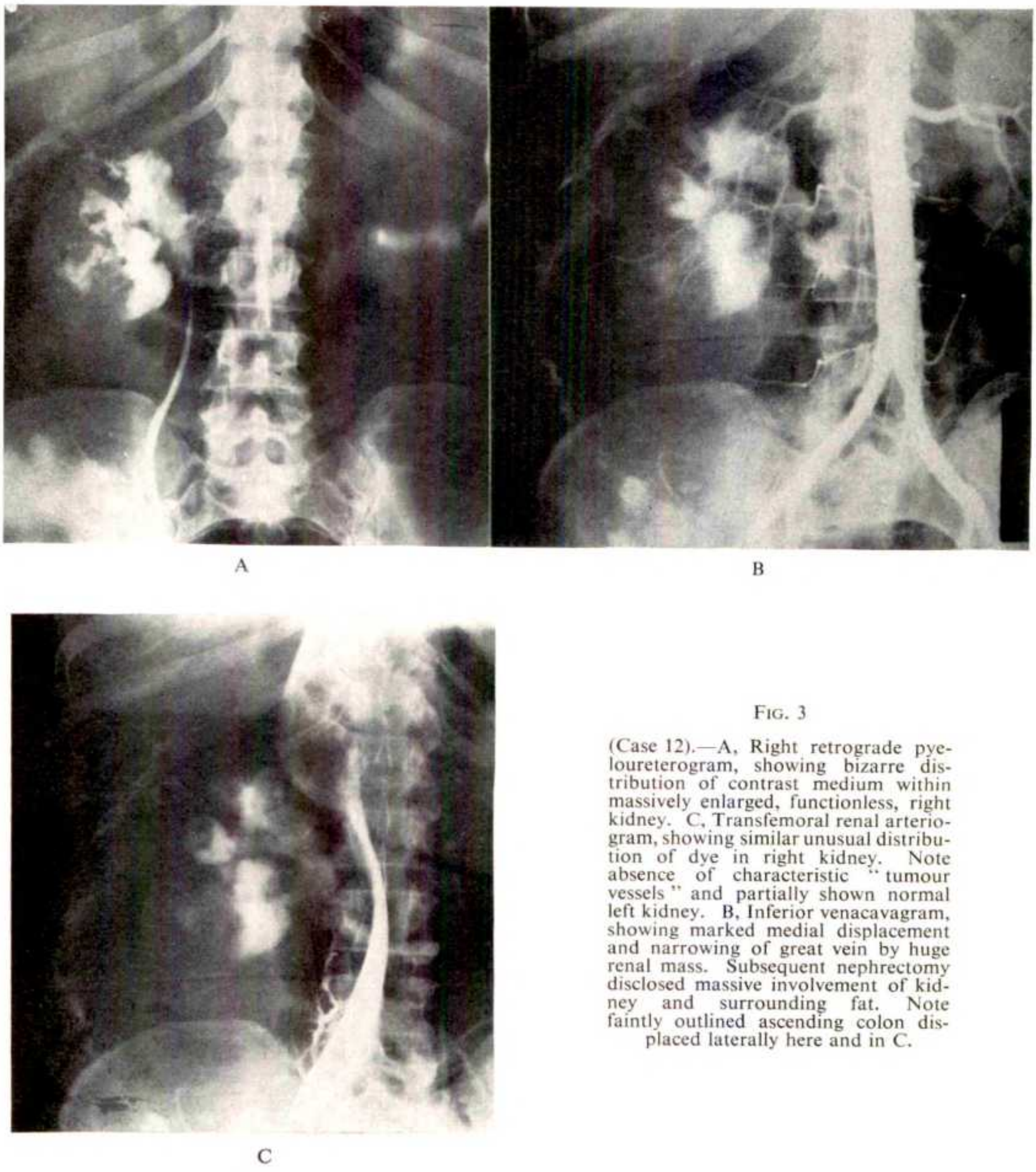
Manifestations of Hepatic Dysfunction in Seven Patients with Xanthogranulomatous Pyelonephritis

Case	Status	Alkaline phosphatase (U/L)	SGOT (U/L)	Prothrombin time (sec.)	BSP retention in 1 hr. (%)	Bilirubin, indirect[1] (mg./100 ml.)	Serum proteins (gm./100 ml.)					
							Albumin	α_1-globulin	α_2-globulin	β-globulin	α-globulin	Total
	Normal values	< 60	< 24	17-19	< 5	< 0·6	3·3-4·3	0·3-0·4	0·5-0·8	0·6-1·1	0·8-1·6	6·0-7·7
9	Preop.	42	11	25	14	0·5	2·03	0·5	1·13	1·22	2·16	7·04
	Postop., 6 mths	27	21	19	0	0·65	3·94	0·34	0·61	1·02	1·76	7·67
10	Preop.	83	30	21	16	0·3	2·75	0·7	1·11	0·93	1·52	7·01
	Postop., 9 mth.	55	...	19	3·2	0·5	4·14	0·28	0·74	0·83	1·11	7·10
12	Preop.						1·97	0·58	1·01	1·06	2·12	6·74
	Postop., not tested											
13	Preop.	53					2·41	0·49	1·34	1·07	1·78	7·09
	Postop., 1 yr.	42					3·31	0·41	0·71	1·01	1·95	7·39
14	Preop.	42	21	22	6	0·5	2·89	0·42	0·72	1·02	1·23	6·28
	Postop., not tested											
17	Preop.	248	112	...	...	0·6	2·68	0·45	1·15	0·96	1·53	6·77
	Postop., 1 wk.	155	72	24	9	0·3	...	...	...	...	...	...
18	Preop.	103	19	24	25	0·9	2·02	0·63	0·93	0·93	1·97	6·48
	Postop., 1 mth.	65	...	22	0	0·3	2·48	0·44	0·75	1·21	1·71	6·59

[1] No direct bilirubin was detected in tested sera.

bilateral nephrostomies. Renal calculi were present in 6 patients, bilaterally in 2 and unilaterally, in the xanthogranulomatous kidney, in the remaining 4.

In 6 cases, a diagnosis of malignant tumour was entertained pre-operatively (Fig. 3). Of the remaining 12 cases, 5 were diagnosed as hydronephrosis (Fig. 4) or pyonephrosis (Fig. 5), 3 as perinephritis (1 with draining sinus), 1 as intrarenal abscess (Fig. 6), and 1 as renal carbuncle. The remaining 2 patients were suspected of having renal tuberculosis (1 also was suspected of having a renal tumour and the other, a subhepatic abscess).



A

B

C

FIG. 3

(Case 12).—A, Right retrograde pyeloureterogram, showing bizarre distribution of contrast medium within massively enlarged, functionless, right kidney. C, Transfemoral renal arteriogram, showing similar unusual distribution of dye in right kidney. Note absence of characteristic "tumour vessels" and partially shown normal left kidney. B, Inferior venacavagram, showing marked medial displacement and narrowing of great vein by huge renal mass. Subsequent nephrectomy disclosed massive involvement of kidney and surrounding fat. Note faintly outlined ascending colon displaced laterally here and in C.

Operations and Findings.—Exploratory operations were performed in all cases; in 2, because of extensive involvement of the surrounding structures (cases 1 and 5), only a generous biopsy specimen was obtained.

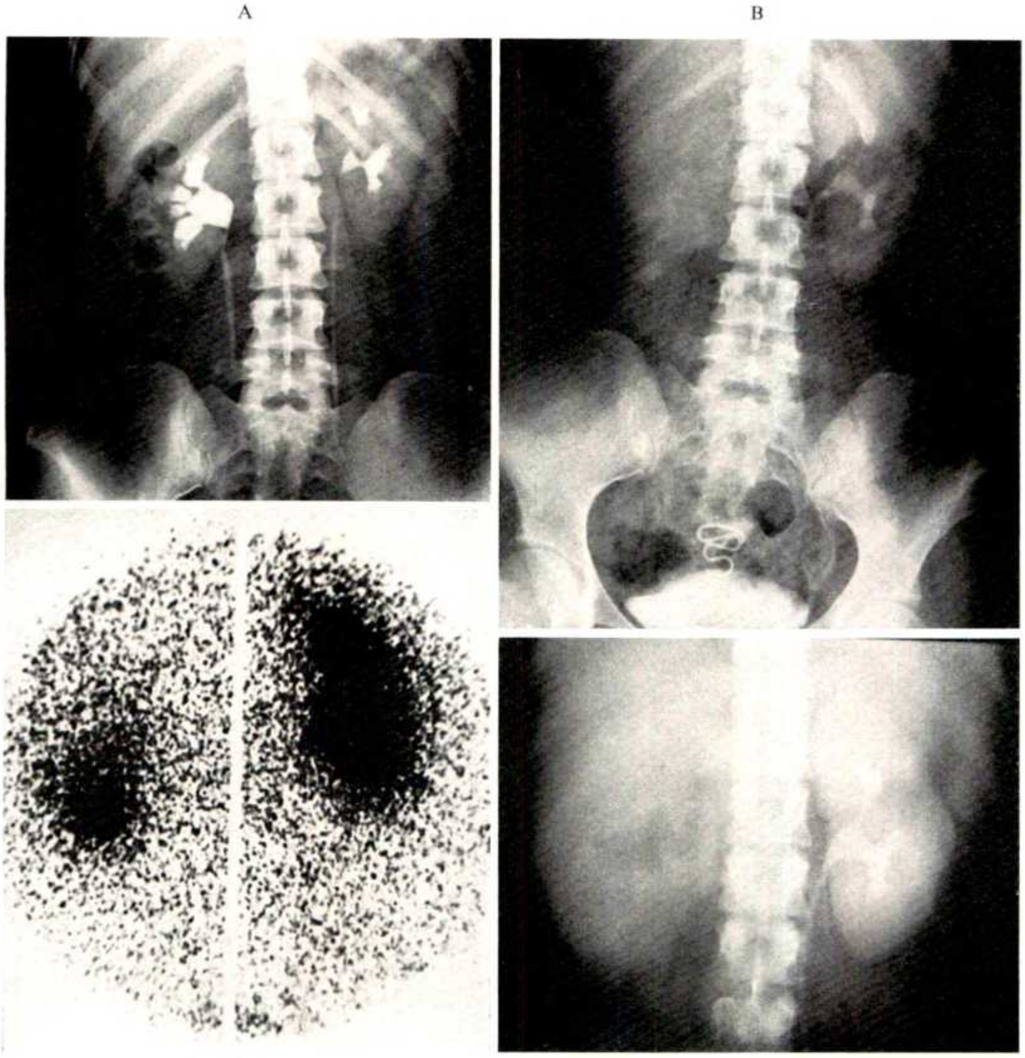


FIG. 4

(Case 17).—A, Excretory urogram, showing bilaterally normal upper urinary tracts with minimal narrowing of right uretero-pelvic junction. B, Excretory urogram 4 years later, showing poorly functioning, hydronephrotic, stone-bearing (lower pole) right kidney. Left kidney is unchanged. C, Radio-iodohippurate (^{131}I) renal scan, showing small amount of functioning right renal parenchyma and equally active normal left kidney. Note "cold area", upper pole of right kidney, corresponding to mass seen on tomogram. Nephrectomy revealed nephric and perinephric xanthogranulomatous pyelonephritis. D, Tomogram at same time as B, showing mass in upper pole of right kidney.

Nephrectomy was performed in 15 cases. In the remaining case a pyocalyx was excised and drained. Perirenal fat, whether or not involved by xanthogranulomatous change, was inflamed, œdematous, firm, and adherent to the diseased kidney in every case.

The characteristic xanthogranulomatous inflammatory process was confined to the kidney in 4 cases; it involved the kidney and Gerota's fat in 13 cases and the kidney and its surrounding fat with widespread retroperitoneal involvement extending down the right paracolic gutter in 1 case. The left renal involvement exceeded the right by a ratio of 12 : 6.

Prognosis.—Three patients were lost to follow-up; the remaining 15 were followed for 2 months to 18 years (mean, 5·6 years); none had an ipsilateral or contralateral recurrence of the disease, and 3 died of unrelated causes.

Fig. 5 (case 16).—Tomogram, showing right pyonephrosis with surrounding thin rim of renal parenchyma (*arrows*) nephrectomy disclosed nephric xanthogranulomatous pyelonephritis. Left kidney is normal.

Fig. 6 (case 15).—A, Retrograde pyeloureterogram, showing intrarenal abscess (*arrow*) with calyceal distortion in mid-portion of right kidney. B, Excretory urogram 6 months after excision, drainage, and closure of involved calyceal infundibulum (*arrow*).

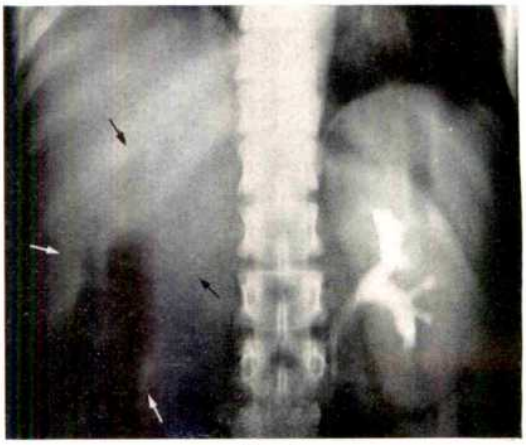
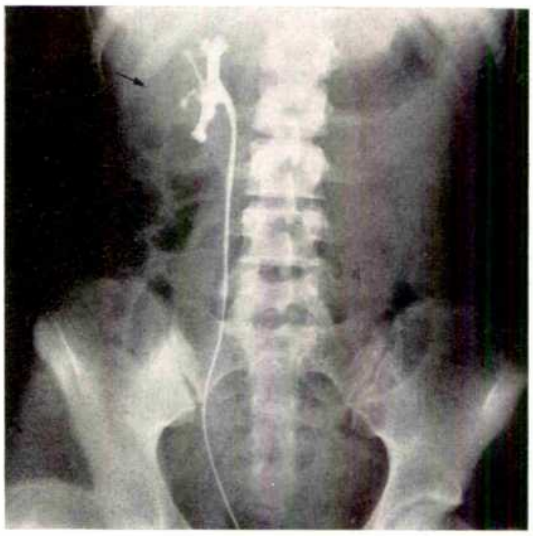
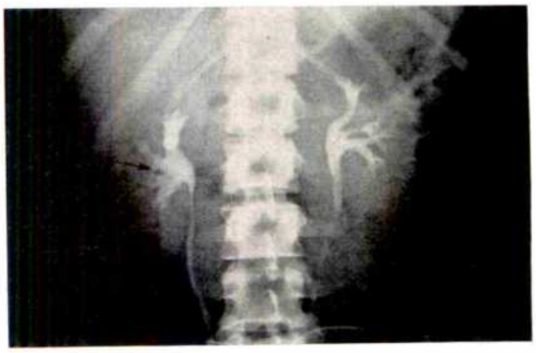


FIG. 5





A FIG. 6 B

DISCUSSION

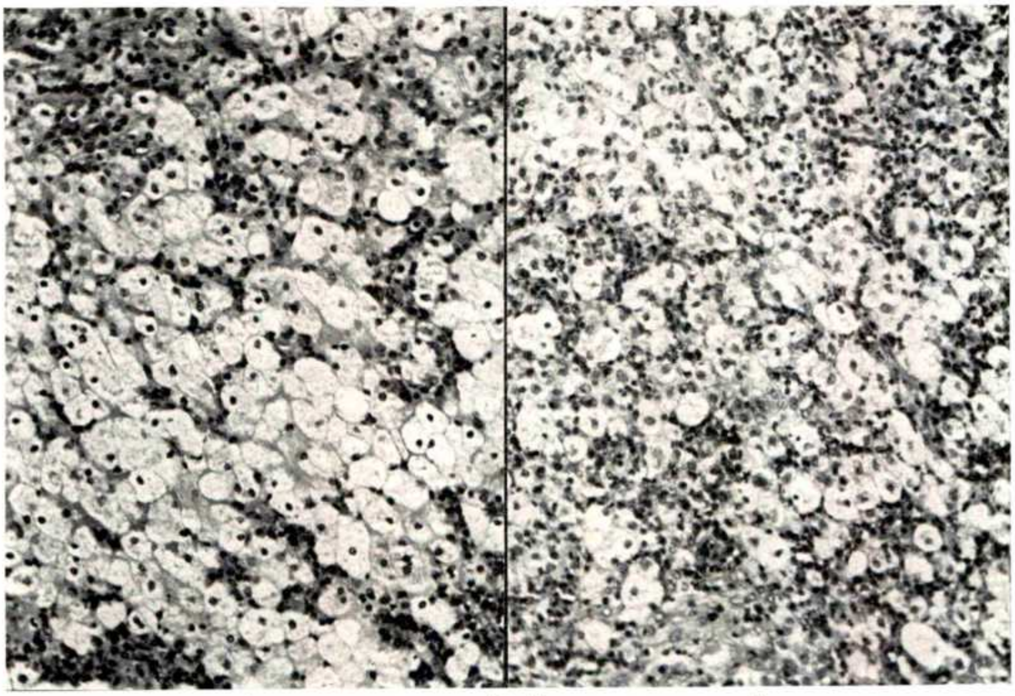
Xanthogranulomatous pyelonephritis is a rare entity (18 instances among 3,000 cases of chronic pyelonephritis) and, despite its reported preponderance in the female (70 per cent according to Anhalt *et al.* (1971), the sexes were equally affected in our series. Most cases occur in the fourth through sixth decades but neither infants nor the aged are spared (Noyes and Palubinskas, 1969; Ceccarelli *et al.*, 1970).

There are no pathognomonic clinical manifestations nor are there any characteristic physical findings. Most patients have multiple genito-urinary manifestations and commonly present with renal pain, low-grade fever with or without chills, and generalised vague illness with weight loss. Less commonly, lower tract irritation, hæmaturia, or flank sinus which has failed to close post-operatively is the presenting complaint.

A history of previous obstructive uropathy, calculous disease, and urologic procedures, obtained in two-thirds (12/18) of our patients, may be of some value and should certainly be kept in mind.

Physical examination commonly discloses a renal mass (14/18), hepatomegaly (6/18), and, rarely, a draining flank sinus (1/18). Hypertension, reported in 45 per cent of cases by Anhalt *et al.* (1971), was noted in 2 of our patients.

Cultures of renal tissue invariably are positive but the bacterial spectrum may differ considerably from that of the bladder urine; indeed, in over half of our cases (7/13) the bladder urine was sterile. The therapeutic implications of such bacteriologic differences in critically ill patients are self-evident.



A FIG. 7 B

A, (Case 12), Inflammatory reaction characterised by foamy xanthomatous histiocytes simulating clear cell renal carcinoma. (Hæmatoxylin and eosin. × 120.) B, (case 11), Xanthomatous inflammatory reaction mixed with polymorphonuclear leukocytes. (Hæmatoxylin and eosin. × 120.)

The commonest uropathogens are *E. coli*, *Proteus*, and *Pseudomonas*. A newly described *Pseudomonas* species, *Pseudomonas cepacia*,[1] formerly known as group IV-D gram-negative bacillus, was the cause of severe renal sepsis in the young man suspected of having renal tuberculosis (case 14) and responded well to 2 weeks of tetracycline therapy post-operatively.

The association of reversible hepatic dysfunction, manifested in 15 per cent of patients with hypernephroma without metastasis (Warren *et al.*, 1970), with xanthogranulomatous pyelonephritis in 7 of our patients is of great interest. It further substantiates the opinion of Vermillion *et al.* (1970), who reported 2 of the above cases (cases 9 and 10), that the syndrome is more likely

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[1] J. A. Washington II, Department of Microbiology, Mayo Clinic: personal communication.

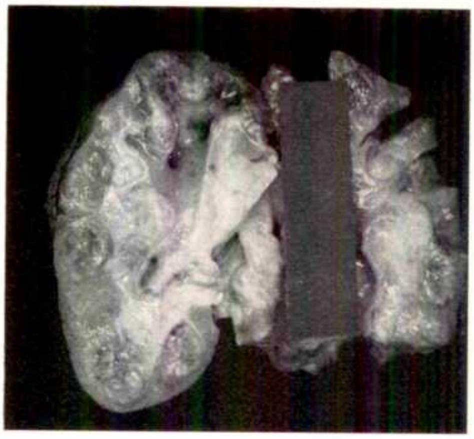


FIG. 8

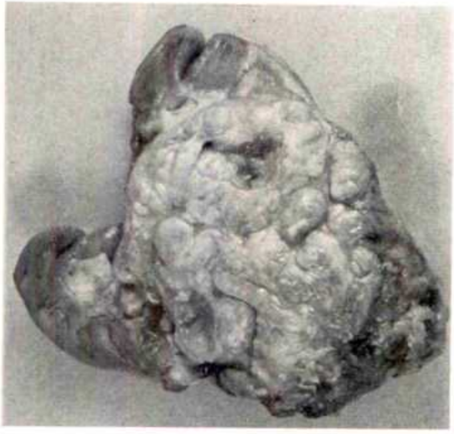
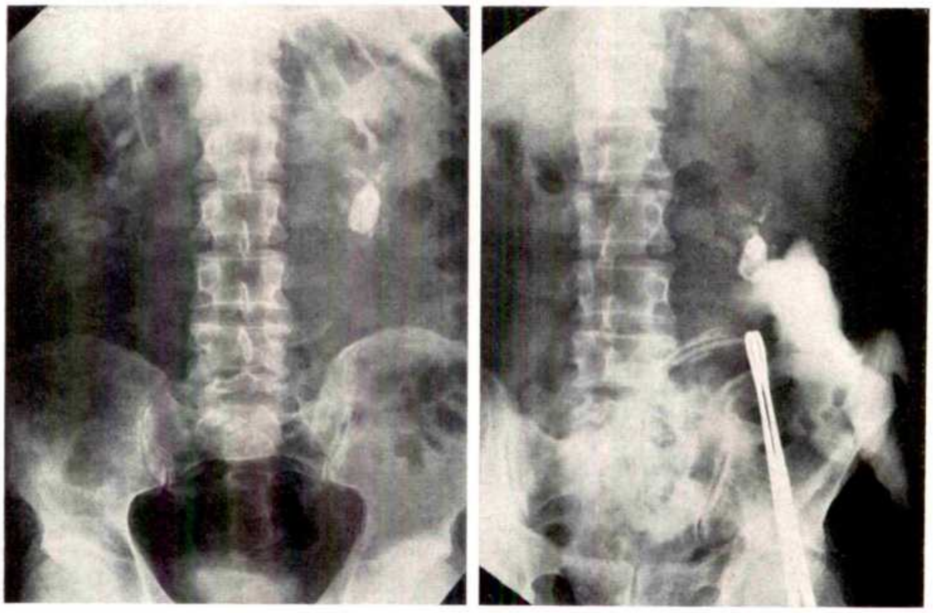


FIG. 9

Fig. 8 (case 7).—Multiple foci of xanthogranulomatous pyelonephritis involve renal pyramids but confined to kidney (stage I). (From Selzer, D. W., Dahlin, D. C., DeWeerd, J. H.: Tumefactive xanthogranulomatous pyelonephritis. *Surgery*, *42*, 874-883, 1957. By permission of the C. V. Mosby Company.)

Fig. 9 (case 6).—Nephric and perinephric xanthogranulomatous pyelonephritis (stage II). This patient presented with draining left-flank sinus. (From Selzer, D. W., Dahlin, D. C., DeWeerd, J. H.: Tumefactive xanthogranulomatous pyelonephritis. *Surgery*, *42*, 874-883, 1957. By permission of the C. V. Mosby Company.)



A FIG. 10 B

(Case 8).—A, Excretory urogram, showing mass adjacent to functionless, stone-bearing lower segment of left duplex kidney. Upper segments are normal bilaterally. Right heminephrectomy had been performed 6 years earlier for nephrolithiasis. B, Outline of left-flank sinus developing after incision and drainage of left-flank mass. Subsequent heminephrectomy (left lower segment) disclosed nephric and perinephric xanthogranulomatous pyelonephritis (stage II), and sinus gradually healed.

the result of renal necrosis rather than of the malignant change *per se*. The data in these 7 patients are incomplete but the general pattern of reversion of abnormal values toward normal soon after nephrectomy is identical with observations in patients with non-metastatic hypernephroma (Warren *et al.*, 1970). On the other hand, abnormalities of lipid or calcium metabolism are not a feature of this diease—a hypercholesteræmic patient had primary myxœdema (case 9) and another with hypercalcæmia had primary hyperparathyroidism (case 18).

Nephrolithiasis of the xanthogranulomatous kidney in this series is much less frequent (22 per cent) than in reported series (70 per cent; Anhalt *et al.*, 1971). Renal masses usually indistinguishable from hypernephroma are found 3 times more commonly than are functionless or hydronephrotic kidneys. Angiographic and nephrotomographic studies as well as radioisotope photo-scanning are useful but not foolproof means of ruling out a malignant lesion; however, the close resemblance of most of the xanthogranulomatous lesions to renal tumour and the pressing nature of the presenting complaints usually lead to an exploratory procedure.

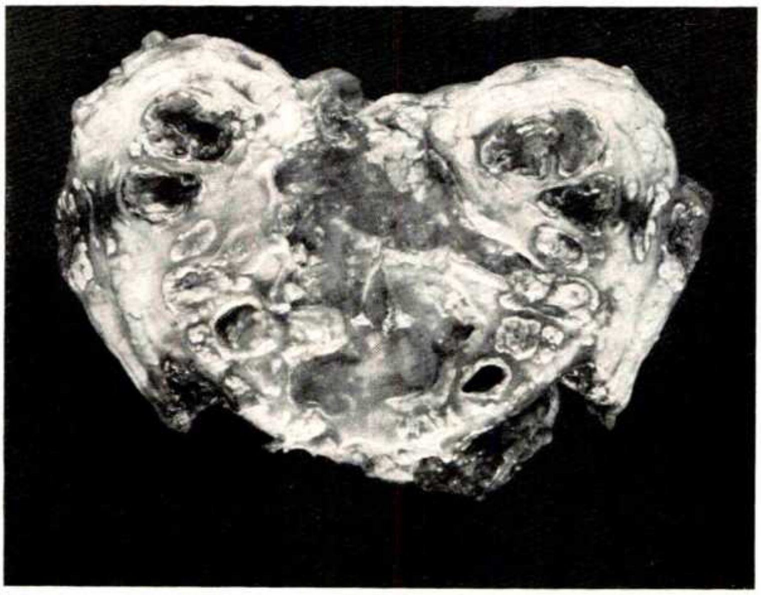


FIG. 11

(Case 12).—Massive involvement of right kidney and perirenal and pararenal (retroperitoneal) fat by xanthogranulomatous pyelonephritis (stage III). Specimen does not show retroperitoneal mass of tissue.

Pathologic features of xanthogranulomatous pyelonephritis have been fully discussed by several authors (Selzer *et al.*, 1957; Tonelli and Giannotti, 1969; Anhalt *et al.*, 1971). The disease essentially represents massive tissue necrosis followed by phagocytosis of the liberated cholesterol and other lipid materials by macrophages. The term " granuloma " should be used in its broadest sense because, in this context, it may simply describe the presence of lipids in macrophages (xanthoma cells) (Fig. 7) without necessarily embracing other features of typical chronic granulomas—for example, epithelioid cells and giant cells.

Xanthogranulomatous pyelonephritis closely mimics renal cell carcinoma, hydronephrosis or pyonephrosis with or without calculi, renal carbuncle, and tuberculosis or other specific granulomas with draining flank sinuses and may justifiably be called " the great imitator ".

Despite claims to the contrary (Anhalt *et al.*, 1971), two-thirds of xanthogranulomatous lesions, in our experience, are associated with a functioning kidney and, in such instances, conservation of the viable nephrons, especially in a young patient, is the procedure of choice. More extensive lesions are usually treated by removal of the kidney and the involved perinephric tissues.

Xanthogranulomatous pyelonephritis may be classified into 3 stages:

Stage I. Nephric. The renal parenchyma contains little fat. Thus, the finding of an xanthogranulomatous process without perirenal involvement is unusual and is a manifestation of a central abscess with necrosis and tissue breakdown (Fig. 8) (4 cases in this series). Local excision and drainage, if enough viable renal parenchyma can be left behind, may suffice (as in case 15; see Figure 6).

Stage II. Nephric and Perinephric. Involvement of Gerota's perinephric fat is invariably accompanied by nephric xanthogranuloma and resembles a renal carbuncle (Fig. 9) (14 cases). Most cases require nephrectomy but a few may lend themselves to local excision (case 8; see Figure 10).

Stage III. Nephric, Perinephric, and Paranephric. The kidney, Gerota's fat, and the paranephric or retroperitoneal fat are involved, representing a massive spread of the disease (Fig. 11) with much distortion of the neighbouring structures. Radical removal of the diseased kidney encased in a mass of xanthogranulomatous tissue extending down the paracolic gutter is the treatment of choice (case 12). Apparently " inoperable tumours ", later found to be xanthogranulomas, were only biopsied in 2 instances (cases 1 and 5) with no ill effects in the one case followed for 15 years.

Xanthogranulomatous pyelonephritis is a unilateral disease and, although in our series the left kidney was involved much more frequently than the right, in general there is no side of predilection (Anhalt *et al.*, 1971). The disease does not recur and the prognosis in patients with a normal contralateral kidney is excellent.

SUMMARY

Eighteen patients with xanthogranulomatous pyelonephritis were treated at the Mayo Clinic during the past 53 years. The variable and often deceptive rœntgenographic appearances, often matched by diagnostic inaccuracies confounded by a hepatic dysfunction syndrome akin to that produced by renal cell carcinoma, are often associated with equally confusing and diverse manifestations of the disease closely mimicking those of hypernephroma, perinephric abscess, pyelonephritis with stone, renal carbuncle, and tuberculosis of the kidney. The common denominator is renal sepsis with localised or widespread necrosis and abscess formation. Three different stages of the disease and suitable methods of treatment for each are described. The disease follows a benign course. There are no recurrences and the results of treatment are most gratifying.

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British Journal of Urology (1972), **44**, 309-310

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MULTILOCULAR RENAL CYST WITH INTRA-PELVIC HERNIATION OF A DAUGHTER LOCULE

By LORRAINE SMITH, M.B., Ch.B., D.M.R.D.

University College Hospital, Gower Street, London W.1

MULTILOCULAR renal cyst is a rare disease. The present case is unusual in that pyelography 20 years before indicated the kidney was essentially normal.

CASE REPORT

B. S., a 50-year-old woman of British extraction, presented because of an asymptomatic mass in her right abdomen. Routine investigations including a blood screen, urine examination and blood urea estimation were all normal. Intravenous urography demonstrated a large right kidney measuring 16·5 cm. in length, with a large mass

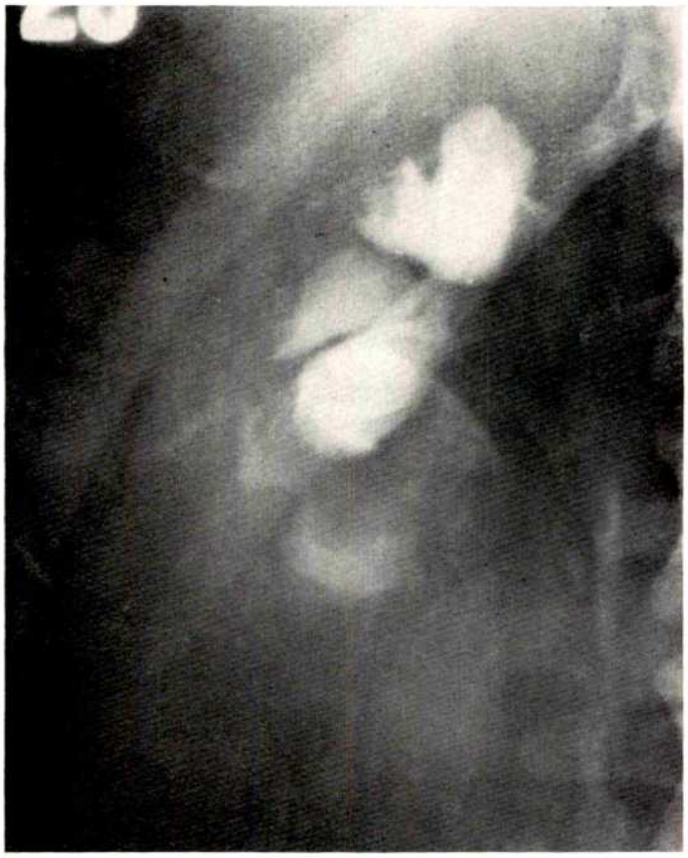

FIG. 1

Intravenous pyelogram (20 min. film) demonstrating a translucent filling defect in the renal pelvis, with contrast in a normal sized ureter distal to this. The renal calyces are dilated and there is a mass occupying the lower pole of the right kidney.

in the lower pole displacing dilated lower calyces and with a constant filling defect in the right renal pelvis. The left kidney was duplicated but was otherwise normal.

Urography done 20 years before showed a normal right kidney at that time. A staghorn calculus present in the lower moeity of the duplicated left kidney was subsequently removed by pyelolithotomy.

Aortography revealed an avascular space-occupying lesion of the right renal pole which had the characteristics of a large simple cyst. Several clusters of small irregular vessels, seen best in the venous phase and just below the renal pelvis, were considered to be possibly indicative of the presence of a malignant tumour and nephrectomy was advised.

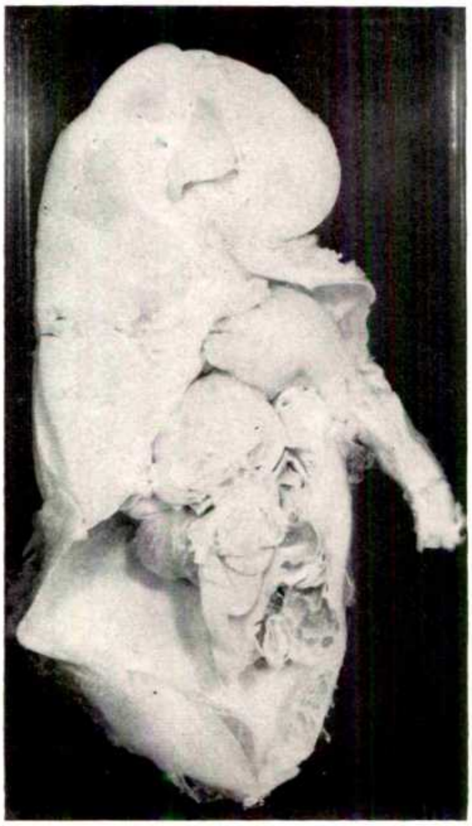

FIG. 2

The right kidney, which measured 16 cm., showing the multilocular nature of the cyst. One of the daughter locules is seen impacted at the uretero-pelvic junction.

At nephrectomy the right kidney measured 16 cm. The upper pole had a normal appearance but the calyces were a little dilated and the papillæ blunted. There was an irregular smooth-surfaced fleshy mass, approximately 5 cm. wide, impacted at the right uretero-pelvic junction and almost filling the dilated pelvis. At the lower end of the pelvis the mass blended with kidney tissue which was cystic and multilocular and a large 5 cm. thin-walled cyst occupied the lower pole.

Histological Examination.—The pelvic mass was cystic. The multilocular intra-renal cysts were lined by low cuboidal or flattened epithelium. The cyst septa contained abdundant cellular mesenchyme with small areas of hæmorrhage present. Although the mesenchyme was excessively cellular in places, no mitoses were demonstrated.

SUMMARY

A case of multilocular renal cyst with intrapelvic herniation of a pedunculated daughter locule in a woman who had previously had normal intravenous urography.

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RENAL AND PERIRENAL EMPHYSEMA

By S. COSTAS, F.R.C.S.(Ed.)[1]

University of the Witwatersrand Medical School

GAS formation, associated with infection, is indicative of a serious life-threatening illness. In urological practice, clinical or radiological evidence of gas has been reported in three main situations: (1) Infection by anaerobic spore-bearing bacilli, consequent to urological operations as reviewed by Winstead (1952) and Goldstein and Abeshouse (1934). (2) Cystitis emphysematosa, or gas in the bladder, either due to infection or a communicating fistula. (3) Gas in the upper urinary tract or in the substance of the kidney due to infection or to entrance via pathological communication with the gastro-intestinal tract, lung or skin.

The first case of gas-forming infection in the kidney, diagnosed clinically, appears to be that of Kelly and MacCallum (1898). The gas was demonstrated by ureteric catheterisation and subsequent drainage of an infected kidney. The first radiological diagnosis of renal emphysema seems to have been made by Randall, as reported by Schultz and Klorfein (1962) and by Stokes (1966).

Three cases of gas forming infection in the upper urinary tract diagnosed radiologically are herein reported and reviewed together with 31 similar cases in the literature.

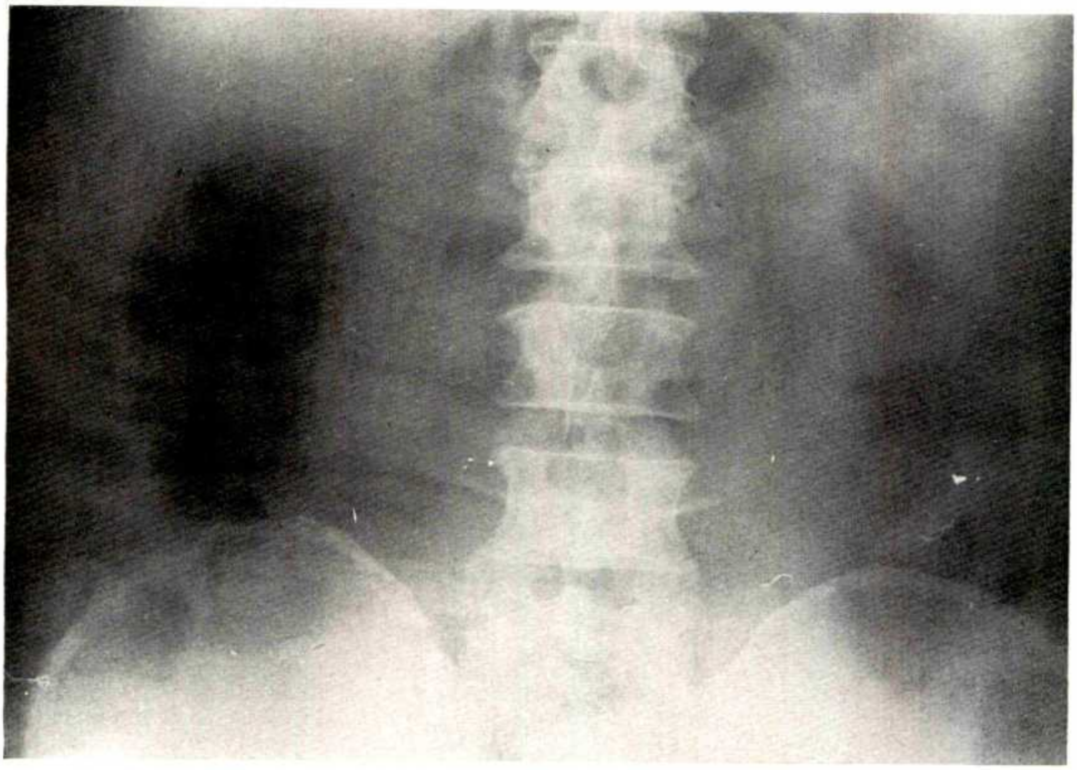

FIG. 1

Case 1. Abdominal X-ray. Gas containing abscess in right loin.

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CASE REPORTS

Case 1.—Mr L., aged 78 years. In January 1968 this patient had a total cystectomy and ileal conduit for a carcinoma of the bladder. At follow-up he remained well except for unexplained episodes of right-loin pain. He was transferred to our hospital on the 14th June 1969 from a peripheral hospital, where he had been treated for 6 days for acute pyelonephritis. On examination he was extremely lethargic and had acidotic respiration. He was apyrexial, pulse 84 and B.P. 150/70 mm. Hg. Marked tenderness was noted in the right loin. No mass could be felt nor crepitus elicited. Blood urea 372 mg./100 ml., Serum sodium 123 mEq./l. Chlorides 95 mEq./l., Potassium 5·8 mEq./l. and CO_2 content 7 mEq./l. Urine culture showed an infection by Proteus mirabilis and there was no glycosuria. A plain X-ray of the abdomen showed an unusual gas shadow in the right loin (Fig. 1). The patient's infection, electrolyte imbalance, acidosis and uræmia were controlled by appropriate therapy. Sixteen days after admission an intravenous pyelogram demonstrated bilateral excretion of the radio-opaque medium which was poorly concentrated on the right and persistence of the gas collection which appeared to lie adjacent to, but outside, the kidney substance (Fig. 2). A "conduitogram" showed free reflux of dye, a little passing through the kidney substance into the gas-filled cavity. A gastrografin enema demonstrated a normal colon lying anterior to the abscess cavity. The abscess was drained with free escape of gas and removal of a large amount of slough from which Proteus mirabilis and E. coli were cultured. During this period urine examinations showed, on rare occasions, a trace of glycosuria. His glucose tolerance curve was in keeping with early diabetes mellitus. The development of trophic ulceration of the feet, due to vascular insufficiency necessitated amputation of the right leg. On eventual discharge, intravenous pyelography showed no evidence of any residual cavity and the infection appeared to be under control.

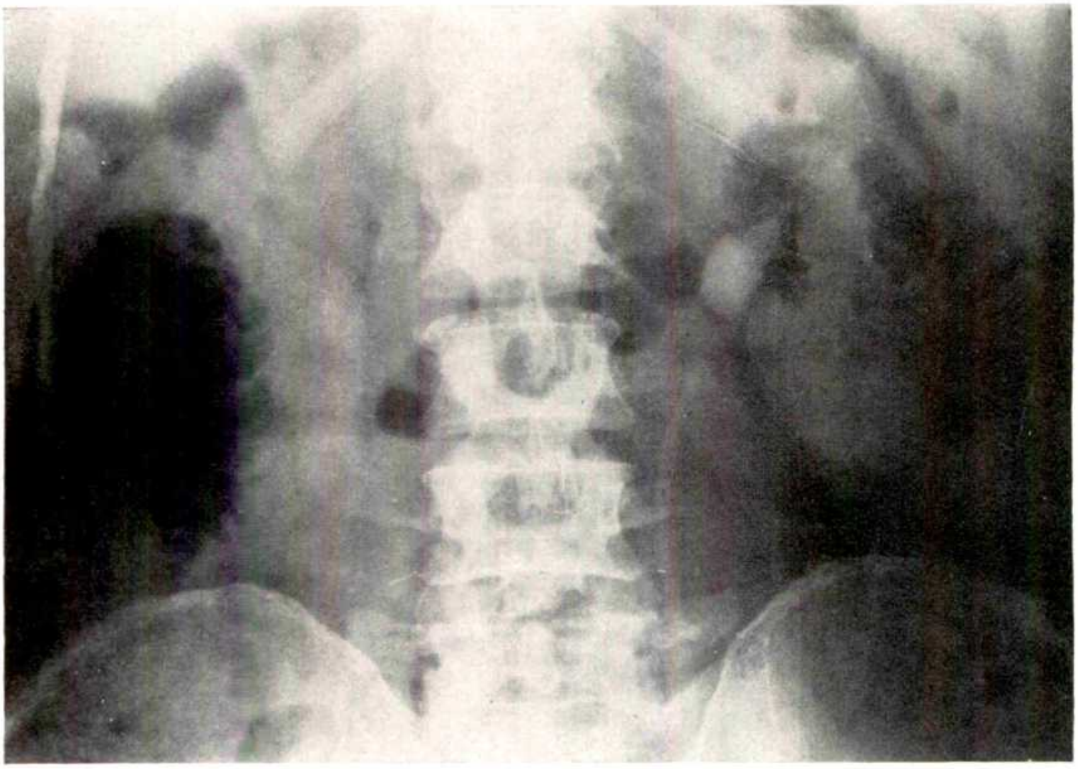

FIG. 2

Case 1. Intravenous pyelogram. Decreased concentration on the right with the gas containing perinephric abscess.

Case 2.—Mrs S., aged 62 years. The patient had been diabetic for 27 years, controlled on 20 u. soluble insulin and 20 u. protamine zinc insulin daily. The diabetes was complicated by retinopathy, peripheral neuritis and possibly peripheral vascular disease. Her urological history dated from childhood, with recurrent attacks of urinary tract infection. At the age of 57 a right hydronephrotic kidney was removed. At this stage the left kidney appeared structurally and functionally normal. Two years later she was found to be hypertensive with a blood urea of 46 mg./100 ml. She had been admitted in February, 1969, with a urinary tract infection due to E. coli. Her blood urea was now 74 mg./100 ml. and an intravenous pyelogram was reported as showing poor concentration but no definite pathology. On admission in October 1969, for excision of a benign breast lump, a blood pressure of 210/120 and a blood urea of 96 mg./100 ml. was recorded. Three days following discharge from hospital she was again admitted (8th November, 1969), with a history of sudden onset of left ureteric colic and anuria of 24 hours' duration. On examination she was in acute pain, clinically acidotic and having rigors. Blood pressure was 100/70 mm. Hg, temperature 99°F. and her extremities were cold. Abdominal tenderness and guarding were present, most marked in the left loin. The blood urea was 290 mg./100 ml., blood sugar 143 mg./ml., hæmoglobin 15·7 g./100 ml. and white cell count 12,000/cm. A clinical diagnosis of calculus obstruction with superimposed infection was made and following administration of intramuscular Ampicillin, 2 ureteric catheters were passed with some difficulty and pus was drained, but a flow of urine was not obtained. X-rays showed a stone in the left lower ureter and the left collecting system filled with gas (Fig. 3). The patient's condition deteriorated progressively and she died 4 hours later, in septicæmic shock. Postmortem showed a kidney weighing 300 g. with macroscopic papillary necrosis and marked softening. This was confirmed on histology which also showed concomitant abscess formation and microcysts, hyaline arteriolar sclerosis and basement membrane thickening in the tubules and glomerulæ. Bacteriological investigations showed an abundant growth of E. coli.

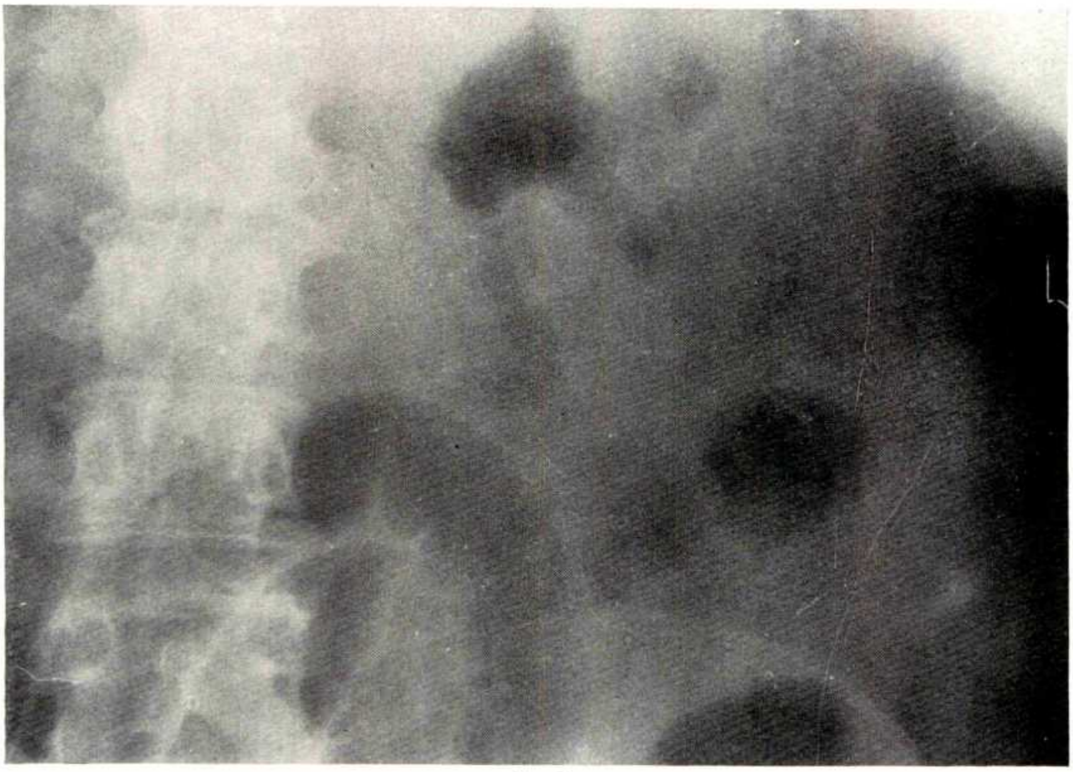

FIG. 3

Case 2. Control film. Gas outlining calyces, pelvis and ureter.

Case 3.—Mrs Z., aged 54 years. This patient had a long history of excessive alcohol intake. Ten years previously she had had a partial gastrectomy and since then had been admitted for hypostatic pneumonia, urinary tract infection and one episode of jaundice. She was admitted in May 1970, with a 5-day history of lower abdominal pain, apparently colicky in nature, which did not radiate but was aggravated by coughing and movement. Other symptoms were anorexia, dysphagia, vomiting and the passage of dark urine. On clinical examination she was found to be poorly nourished, dehydrated and confused. Her temperature was 100·6°F., blood pressure 85/60 mm. Hg and pulse rate 110/min. Examination of the abdomen revealed generalised tenderness and rebound tenderness, most marked over the lower abdomen. Tender masses were palpable in both loins from just below the costal margin of the right mass, crepitus was palpable. Bowel sounds were normal and the abdomen was not distended. She was tender in the recto-vaginal pouch. Urine examination showed no glucose or acetone, one plus of albumen and numerous casts, white and red blood cells. Culture showed E. coli. Her hæmoglobin was 14·7 g./100 ml., white cell count 4,900 and blood urea 108 mg./100 ml. Emergency pyelography demonstrated a poor nephrogram phase bilaterally in what appeared to be large, low-lying kidneys with abnormal gas shadows in the lower pole of the left kidney, and possibly surrounding the right kidney. Intravenous administration of fluids and antibiotic therapy consisting of penicillin, gentamicin and cephaloridine was instituted. Twenty-four hours after admission her hydration and circulatory status was improved. However, she appeared severely toxæmic and was mentally less orientated with a temperature of 104·20°F.

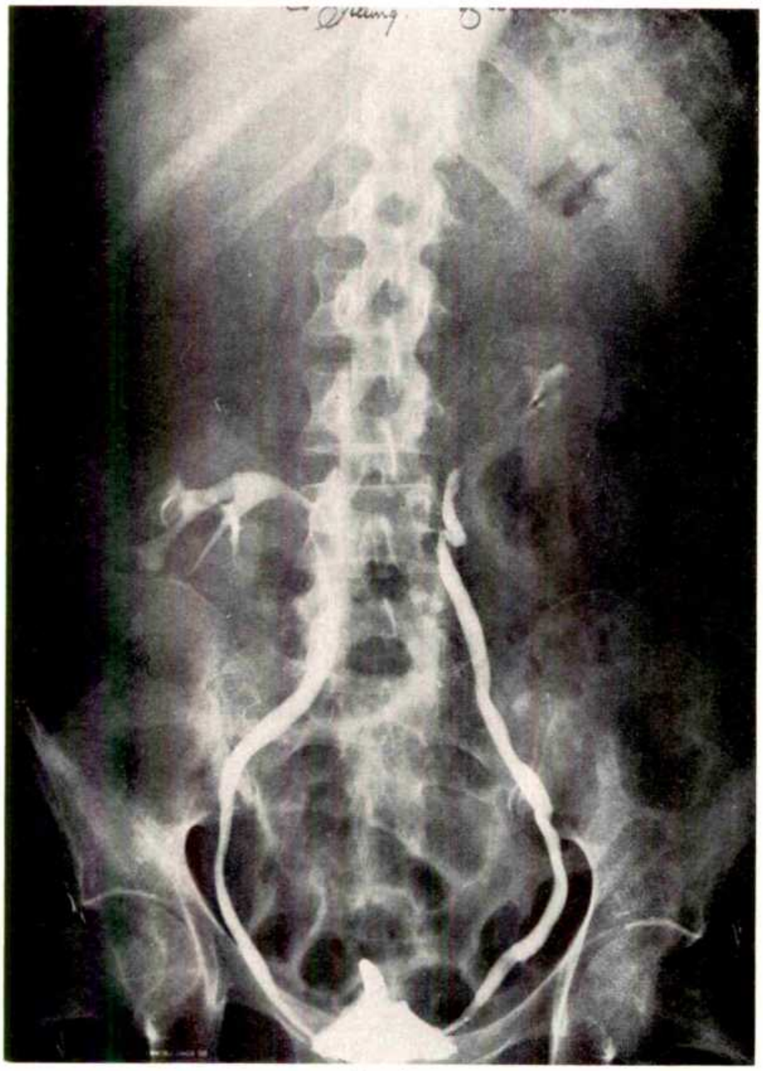

FIG. 4

Case 3. Retrograde pyelogram. Gas containing abscess in the lower pole of left kidney.

She was given 10 mg. Diazepan intravenously and cystoscopy was performed which showed a normal bladder. Retrograde pyelograms showed no obstructive uropathy and confirmed the presence of gas in the lower pole of the left kidney and again suggested the possibility of gas around the right kidney (Fig. 4). Both kidneys were explored under local anæsthesia. These were markedly œdematous and pale. Gas and pus escaped on approaching the surface of the right kidney and a gas-containing abscess was opened in the lower pole of the left kidney. Because of severe bleeding from the friable renal tissue, the wounds were packed with vaginal plugs and drains were inserted. Her post-operative course was complicated by circulatory collapse. Within 12 hours, however, on appropriate therapy, she had a stable circulation and was apyrexial. Her blood sugar was now 600 mg./100 ml. On the 4th post-operative day she passed over a litre of urine for the first time. As her blood sugar showed no tendency to settle spontaneously, small doses of insulin were administered intravenously. Four weeks post-operatively she was well. Her blood urea was 44 mg./100 ml. and her diabetes was controlled by diet alone. Follow-up intravenous pyelography demonstrated a normal right system and on the left complete loss of the calyx and parenchyma in the lower pole.

DISCUSSION

The 3 cases reported illustrate the phenomenon of gas formation in the upper renal tract in three different situations, namely, perirenal, intrarenal and in the collecting system. They were all diabetic and one also had a concomitant urinary tract obstruction.

Of the 34 cases diagnosed radiologically and reported in the literature, 93 were female and 11 male. The age distribution is shown in Table I.

TABLE I

Age Distribution

Age	10-19	20-29	30-39	40-49	50-59	60-69	70-79
No. of patients	1	0	4	5	8	10	6

TABLE II

Associated Disease and Mortality

	Total	Died
Obstructive uropathy	7 (20%)	1 (14·3%)
Diabetes	20 (60%)	8 (40%)
Obstructive uropathy + diabetes	7 (20%)	5 (71%)

Associated Pathology (Table II).—Twenty-one patients (60 per cent) were diabetic and did not have any urological cause to account for the urinary tract infection. Eight (40 per cent) of these patients died as a result of this illness.

Seven cases (20 per cent) were not diabetic but all of these were associated with an obstructing lesion in the urinary tract. Only one of these patients died (14·3 per cent).

In 7 cases (20 per cent) diabetes mellitus and obstructive uropathy were both present with a fatal outcome in 5 of these patients (71 per cent). However, both survivors in the latter group died during the convalescent period. The one, after apparently successful conservative treatment, died as a result of congestive cardiac failure (Harrow, 1963). The other, after having responded well to conservative treatment followed by nephrectomy, died as a result of a myocardial infarct on the 8th post-operative day (Banks *et al.*, 1969).

Two patients were in the early post-partum period when the diagnosis was made, having had urinary tract infections during pregnancy; one patient being a diabetic (Olson, 1957) and the other was shown to have a hydronephrosis (Jenson, 1939).

In all the above patients the causes of obstructive uropathy were; (i) ureteric calculus (7 cases), (ii) ureteric stricture (3 cases), (iii) hydronephrosis (2 cases), (iv) ureteric stone and stricture (1 case), (v) infected cyst of Gartner's duct (1 case, Gillies, 1941).

Clinical Presentation.—Ten patients had a relatively long history suggestive of urinary tract infection. In these cases, the gas was demonstrated during the investigation of an attack of pyelonephritis. In 4 of the cases a mass was present or became palpable during treatment and investigation. Only 2 of these patients died, indicating a somewhat favourable prognosis in this group.

Twenty-one patients showed an acute onset of 3 to 5 days duration associated with nausea, vomiting, rigors and loin pain. In a minority of these patients there was dysuria and increased frequency. Their mental state at the time of admission varied from drowsy to semi-comatose, so that frequently the history had to be obtained from relatives. Twelve (60 per cent) of these 21 patients died. In the remaining 3 cases the rate of onset of the illness is not clear.

Pyrexia of 102°F. or more was present in 10 cases and less than 102°F. in 8. This factor did not appear to influence the prognosis. The blood pressure was only abnormally low in 4 of 12 cases where mentioned. Abdominal tenderness and guarding was a common feature and a loin mass was palpable in 9 cases (42·8 per cent). Bilateral masses were present in case 3 and in a case reported by Harrison (1942). In 2 cases the mass was associated with overlying crepitus (case 3 and Welch, 1949). Palpable crepitus was present in 2 other cases. In one it spread in the subcutaneous tissue of the loin to involve the chest wall and in the second, by spread down the

TABLE III

Causative Organisms

	No. of times cultured
E. coli	20
Aerobactera aerogenes	7
Proteus	5
Klebsiella	4
Pyocyaneus	3
Streptococcus	2
Paracolon bacillus	1

psoas muscle sheath to involve the thigh and inguinal region (Clifford, 1962). Crepitus was always associated with the acute fulminating illness and only the case reported here survived. Although pneumaturia was a clinical feature in the earliest reported cases, it does not appear to be a common symptom.

The bacteria cultured from the urine are shown in Table III. In 10 patients there was a mixed growth of two of these organisms. Whenever blood cultures and/or tissue or pus cultures were taken the same organism as was present in the urine was demonstrated. The radiological distribution of gas in the tissues is shown in Table IV.

TABLE IV

Situation of the Gas

	No. of cases
Renal and perirenal	13
Perirenal	7
Collecting system	7
Collecting system and renal	3
Collecting system, renal and perirenal	2
Renal	2

The 7 cases of perirenal emphysema all occurred in diabetic patients. They illustrate the serious nature of this illness in that 4 patients died (57 per cent). In 5 of these 7 patients, although pus was present, the infection was poorly localised, as shown by the fact that the infective process had extended through the diaphragm in 1 case (Levy, 1953); via the psoas sheath to involve the thigh in another; in the third, to involve the peritoneal cavity (Stokes, 1966) and in the fourth case (as in case 3 above) palpable crepitations were present in the abdominal wall.

The Prognosis.—This is favourably influenced by the early natural history of the disease in that those patients with a slow onset phase show a lower mortality.

The influence of related pathology on the prognosis is shown in Table II.

The relationship of treatment to prognosis in the cases presenting acutely is difficult to assess because of the small numbers. Of 6 patients treated conservatively, only 1 patient survived, but died subsequently of cardiac failure (Harrow, 1963). These patients were invariably very ill but possibly some form of surgical intervention may have been of value, as is suggested by case 3 reported here. Fifteen patients had some form of surgical intervention. Eight survived, the surgery having been performed after a good or partial response to conservative treatment. One died 8 days later as a result of a myocardial infarct (Banks, 1969). In the 7 cases who died following surgery it is noticeable that the spread of the disease was extensive or that the patient had responded poorly to conservative measures. The possibility of surgical intervention being undertaken too early is suggested by case 2.

Some degree of permanent renal damage always follows this type of infection. In 8 patients who survived, subsequent follow-up showed complete destruction of 4 kidneys, severe damage in 2 and less severe damage in two of the cases reported here. Of 18 kidneys studied, post-mortem or after nephrectomy, 11 appeared to have been completely destroyed and 6 showed partial destruction.

CONCLUSION

Gas forming infection in the upper urinary tract or perinephric tissues appears always to be associated either with obstructive uropathy, diabetes mellitus or a combination of the two. The seriousness of this infection is reflected by the high mortality recorded in the literature. Of the associated causes obstructive uropathy *per se* appears to have the lowest mortality, whereas the combination of obstructive uropathy and diabetes mellitus has the highest mortality.

At the time of admission most cases are primarily a septicæmic problem, consequent to their urinary tract infection. They should be treated as such, with adequate antibiotic control, correction of their electrolyte imbalance, treatment of the circulatory collapse and control of the diabetes mellitus, if present. Only then should surgical intervention be contemplated to drain the infection and, if possible, to remove an obstruction if present. Premature surgery could be disastrous, whereas well timed intervention may save life and conserve renal tissue.

SUMMARY

Three cases of renal and perirenal gas-forming infection are presented with an analysis of similar cases in the literature. This serious infection is always associated with obstructive uropathy, diabetes mellitus or a combination of the two. It is associated with a high mortality and loss of renal tissue. The importance of adequate conservative therapy, followed by well-timed surgical intervention is emphasised.

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THE RESULTS OF SURGERY FOR HYDRONEPHROSIS AS DETERMINED BY RENOGRAPHY WITH ANALOGUE COMPUTER SIMULATION

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IT is common experience that reconstructive surgery for hydronephrosis due to long-standing obstruction at the pelvi-ureteric junction gives excellent results in clinical terms but that quite often the radiological result is disappointing in that the degree of calyceal dilatation on intravenous urography may show little if any change following operation. Uncertainty then remains as to whether or not surgery has produced any significant improvement in either renal function or pelvic emptying.

Isotope renography gives more information than urography concerning the function and emptying rate of the individual kidney and in some cases of hydronephrosis simple qualitative assessment of renogram tracings before and after relief of the obstruction may reveal obvious changes in both these parameters; in others, however, visual inspection or measurements of the abnormal renogram curves are inconclusive. Quantitative evaluation of renograms by analogue computer simulation allows more precise comparisons to be made between pre- and post-operative tracings and thus permits valid conclusions to be made concerning the results of pyelo-ureteroplasty.

The present article relates to our experience with 32 children with unilateral pelvic hydronephrosis and with a normal contralateral kidney in whom renography with computer assessment was carried out before and after reconstructive surgery.

CASE MATERIAL AND TECHNIQUES

The ages of the 32 children at the time of operation for hydronephrosis ranged from 12 months to 15 years 4 months. In 29 instances pyelo-ureteroplasty of the Anderson-Hynes type was carried out; in 3, Y-V plasty was performed at the pelvi-ureteric junction.

Isotope renography, employing either I^{131} hippuran in a dosage of 0·5 μc./kg. or, more recently, I^{125} hippuran in a dosage of 0·25 μc./kg. was carried out 2 to 5 days pre-operatively and between 3 and 52 months after operation. The post-operative intravenous urogram was performed as near as possible to the post-operative renogram.

The renograms obtained before and after surgery were compared by analogue computer simulation. The principles and the technique of this procedure have been discussed fully elsewhere (Kathel, 1972). Briefly, the behaviour of hippuran in the body is simulated by the dynamic action of the electronic components in the computer. The computer voltages are made to follow the same laws as those determining the distribution of hippuran in the blood, kidneys and bladder. Thus the computer generates the blood clearance curve, the right and left renograms and the bladder tracing on an oscilloscope (Fig. 1). By adjusting controls on the computer panel the computer-generated " normal " tracing is altered until it matches precisely the tracing obtained from the patient, employing a projection system (Figs. 1 and 2); the degree of deviation of the patient's renogram from the normal is determined from the adjustments needed. The total renal plasma flow and the divided renal plasma flow-rates each expressed as ml./minute, and the rates of collection and evacuation of hippuran by the individual kidneys each expressed as a percentage of the total dosage per minute, can be measured. Changes in these functions after surgery can be ascertained by comparing the results obtained from computer simulation of pre- and post-operative renograms and in this way the effects of operation on the individual kidney can be determined.

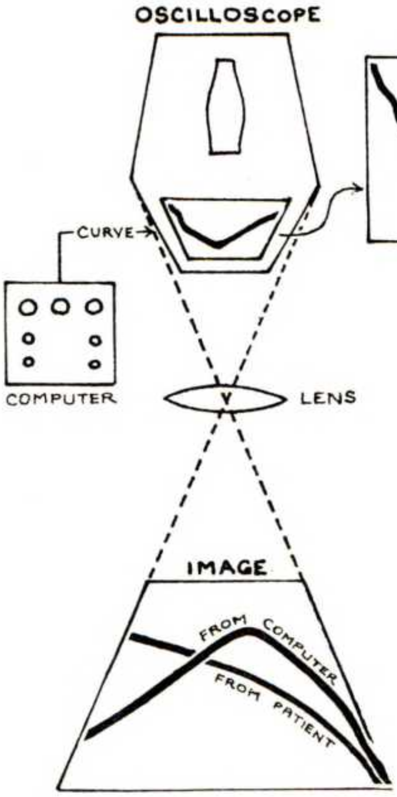


FIG. 1

Fig. 1.—Diagram of projection system. The computer-generated renogram appears on the oscilloscope and is projected so as to superimpose on the renogram obtained from the patient.

Fig. 2.—Adjustment of the computer controls until the computer-generated curve corresponds precisely to the patient's renogram. The deviation of the latter from the former is assessed from the adjustments needed.

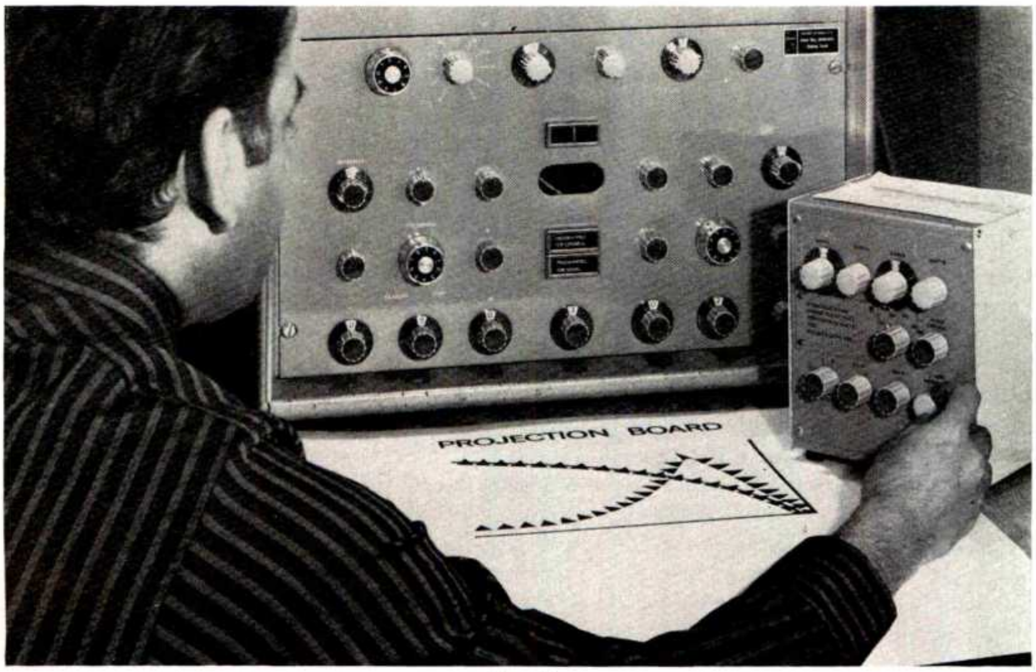


FIG. 2

Results of Surgery for Hydronephrosis

Clinical.—A satisfactory clinical result was obtained in all cases in that each patient was relieved of symptoms. In no case was re-operation needed.

Intravenous Urography.—The pre- and post-operative urograms were compared as regards degree of calyceal dilatation and, in some instances, as regards change in the concentration of contrast medium when this was obvious. Sixteen kidneys were considered to show improvement of various degrees following surgery; 3 had deteriorated and 13 were essentially unchanged.

Visual Assessment of Renograms.—Inspection of the pre- and post-operative renograms from the hydronephrotic kidneys was directed to comparing the general shapes of the tracings and, where possible, to measuring the times taken for the kidney tracings to reach a maximum at the end of the second phase (Tm), which is an index of renal blood flow and tubular function, and the times required for the tracings to fall during the third phase from the maximum to half that level ($T\frac{1}{2}$), which is an index of the rate of tubular and pelvic emptying. Before surgery the tracings were either continually rising, flat or showing severe delay in the third phase (Figs. 3, 4 and 5) so that Tm was measurable in only one instance and $T\frac{1}{2}$ was measurable in none.

After operation, in 10 instances Tm ranged from 2 to 23 minutes; in the remaining 22 it was not measurable. $T\frac{1}{2}$ could be determined in 9 tracings; it varied from $11\frac{1}{2}$ to 34 minutes. Thus in 9 of the 32 cases visual assessment of the renogram curves demonstrated undoubted improvement in kidney emptying after surgery, whilst in the remainder no definite conclusions could be reached although in some a slight to moderate increase in the third phase decline was apparent. Because of the very abnormal shapes of the renograms a valid visual interpretation of changes in tubular function was not considered possible. Of the 9 kidneys showing obvious improvement on renography, intravenous urography showed improvement in 6, no change in 2 and slight deterioration in 1.

Computer Assessment of Renograms

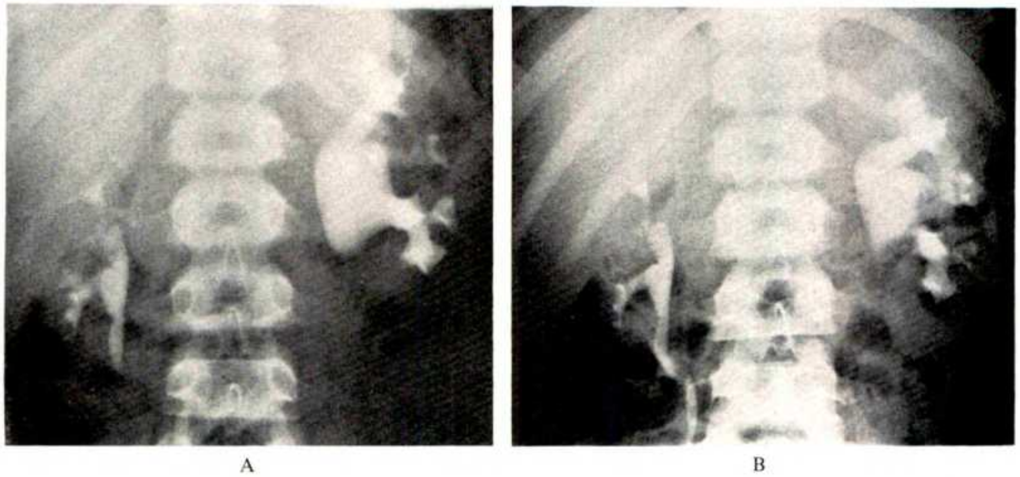
Renal Plasma Flow Rates.—Before operation the plasma flow to the hydronephrotic kidney was less than that to the opposite normal kidney in 17 instances, the same in 11 and greater in 4.

Following operation the flow rate to the hydronephrotic kidney increased in 31 cases. In 23, however, the increase was proportionate, or less than proportionate, to the increased flow to the contralateral kidney consistent with the growth of the child. In 8 cases the flow to the hydronephrotic kidneys was increased disproportionately in excess of the alterations in flow to the normal kidneys. In 1 case the plasma flow to the diseased kidney decreased after operation.

Rates of Collection of Hippuran by the Kidney.—Before operation this measurement, which is an index of renal plasma flow and of renal tubular function, was less in the hydronephrotic kidney than in the normal in 30 cases, greater in 1 and the same in 1.

After operation the rate of collection by the diseased kidney increased in 23 cases, the ratio of increase ranging from 0 : 4·8 per cent/minute to 8·1 : 8·5 per cent/minute. In 3 cases the rate decreased after surgery and in 6 it was unchanged.

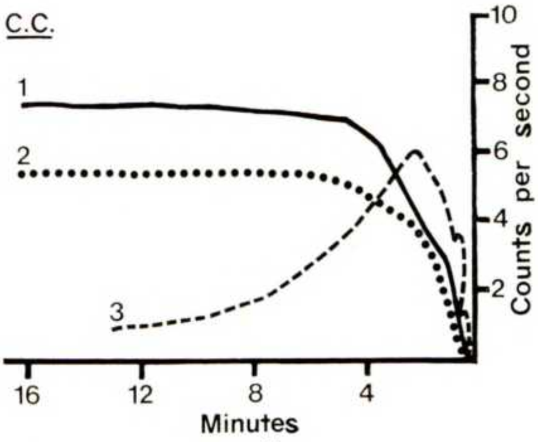
Rates of Evacuation of Hippuran from the Kidney.—Before surgery the rate of evacuation of hippuran from the hydronephrotic kidney was less than that from the normal in all cases. The ratio between the abnormal and the normal ranged from 0 : 24·8 per cent/minute to 20 : 24 per cent/minute. In 29 of the hydronephrotic kidneys the rate of emptying increased after operation; the greatest proportionate increase was from 0 to 17 per cent/minute whilst the least was from 15 to 16 per cent/minute. In 2 cases the rate was unaltered and in 1 it decreased.



A B

FIG. 3.—Left hydronephrosis in 8-year-old girl.

A, Intravenous urogram before operation. Dilated pelvis. Mild calyceal clubbing. B, After operation. Improved calyceal outlines. C, Isotope renograms. Line 1; left kidney before operation: rising tracing. Line 2; after operation; slight decline after peak. Line 3; normal right kidney tracing. Computer analysis of the renograms is shown in Table I.



C

TABLE I

C. C.	Total renal plasma flow ml/minute	Divided renal plasma flow ml/minute		Collection rate %/minute		Evacuation rate %/minute	
		Right	Left	Right	Left	Right	Left
Before operation	320	150	170	8·5	5·8	24·8	6·5
After operation	360	180	180	8·3	6·2	24·8	10·4

Computer analysis of pre- and post-operative renograms in Case 1.

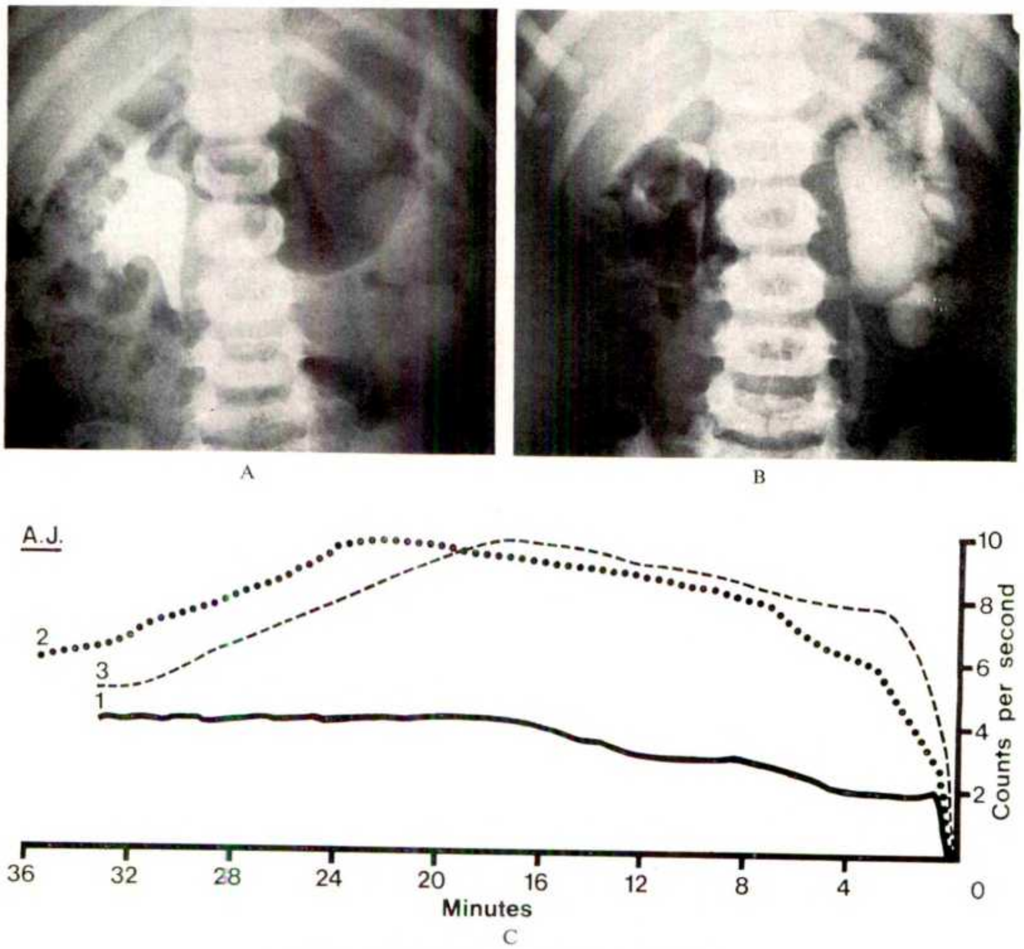


FIG. 4.—Left hydronephrosis in 4½-year-old boy.

A, Intravenous urogram before operation. Severely dilated calyces. B, After operation. Improvement in calyceal dilatation. C, Isotope renograms. Line 1; left kidney before operation; rising tracing. Line 2; after operation; the three phases are present but each is slow. Line 3: right kidney; also shows some delay in phase 2. Computer analysis of the renograms is shown in Table II.

TABLE II

A. J.	Total renal plasma flow ml./minute	Divided renal plasma flow ml./minute		Collection rate %/minute		Evacuation rate %/minute	
		Right	Left	Right	Left	Right	Left
Before operation	145	102	44	5·5	0	14	0·9
After operation	170	93·3	76·5	7·0	4·8	19·8	8·1

Computer analysis of pre- and post-operative renograms in Case 2.

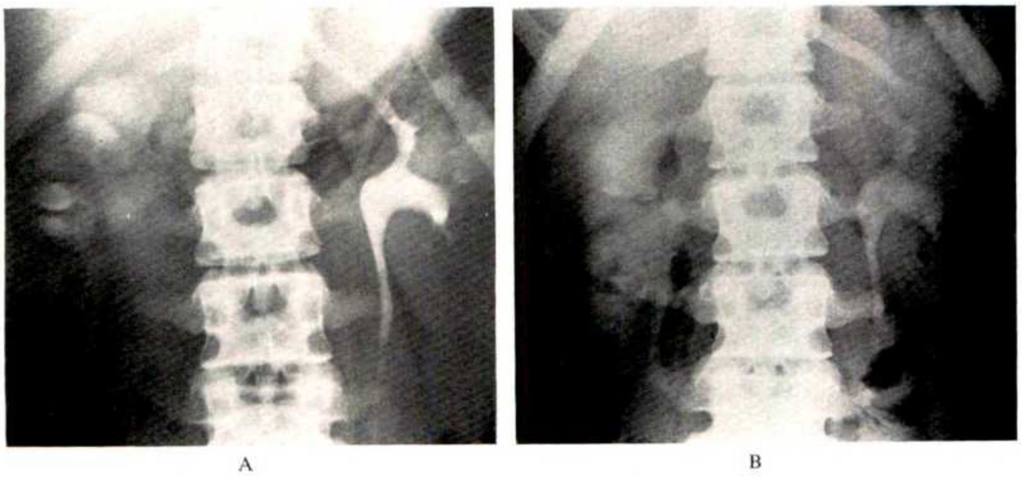


FIG. 5.—Right hydronephrosis in 15-year-old boy.

A, Intravenous urogram before operation. Severe calyceal dilatation. B, After operation. No obvious change in calyces. C, Isotope renograms. Line 1: right kidney before operation; flat tracing. Line 2: after operation; very slow rise and decline. Line 3: normal left kidney tracing. Computer analysis of the renograms is shown in Table III.

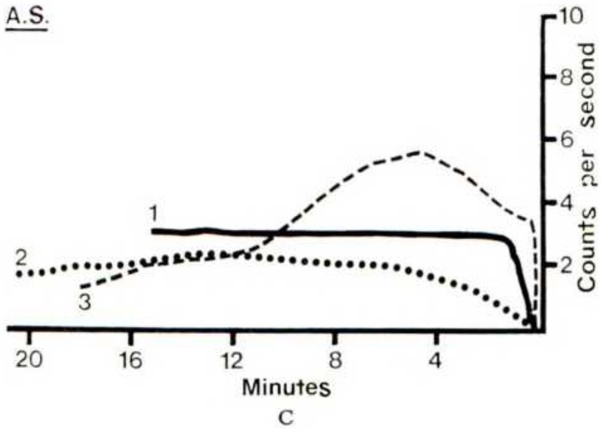


TABLE III

A. S.	Total renal plasma flow ml./minute	Divided renal plasma flow ml./minute		Collection rate %/minute		Evacuation rate %/minute	
		Right	Left	Right	Left	Right	Left
Before operation	390	136·5	253	0	6·3	5·0	24
After operation	400	147	233	4·6	6·3	15·0	24

Computer analysis of pre- and post-operative renograms in Case 3.

Illustrative Cases

Case 1.—C. C., a girl aged 8 years, presented with loin pain due to a left hydronephrosis. Intravenous urography 10 months after pyelo-ureteroplasty showed some improvement in the outlines of the calyces which had previously been mildly blunted (Fig. 3*a* and 3*b*). Isotope renograms from the hydronephrotic kidney (Fig. 3*c*) before and after operation rose to a plateau and in neither tracing was T½ measurable. The renogram from the right kidney was normal. Computer analysis of the pre- and post-operative renograms is shown in Table I. This demonstrates increases in the collecting and emptying rates in the diseased kidney after operation.

Case 2.—A. J., a boy aged 4½ years, had a severe left hydronephrosis (Fig. 4*a*). Intravenous urography 6 months after surgery showed improved concentration and a lessening of calyceal dilatation (Fig. 4*b*). The pre-operative renogram (Fig. 4*c*) from the diseased kidney showed a continually rising tracing; in the post-operative curve the three renogram phases were present but each was delayed. Computer analysis of the renograms (Table II) demonstrated improvement in renal blood flow and in collecting and emptying rates after surgery.

Case 3.—A. S., a boy aged 15 years, had a severely hydronephrotic right kidney (Fig. 5*a*). Intravenous urography 5 months after pyelo-ureteroplasty showed no obvious change in the calyceal outlines (Fig. 5*b*). Renography of the affected kidney before operation (Fig. 5*c*) gave a flat tracing. After operation the curve showed a slow rise and decline. Computer analysis of the renograms (Table III) demonstrated improvement in renal plasma flow and in collecting and emptying rates after surgery.

DISCUSSION

Isotope renography is an attractive test of individual kidney function since it provides, by a simple technique, an index of the renal blood flow, of the excretory function of the tubular cells and of the emptying ability of the tubules and the kidney pelvis. The range of normality of renogram tracings is fairly wide but, provided the test is carried out under standard conditions especially as regards the hydration of the patient, repeated renography from the same stable kidney is reproducible to a significant degree. Quantitative assessment of the isotope renogram by visual inspection is, however, difficult and this has limited the value of the test in detecting changes occurring in pathological kidneys over periods of time. In attempts to overcome this drawback, several authors (Krogsgaard and Friis, 1964 and Dawborn and Doyle, 1963) have measured such parameters as the amplitude of the curve in relation to isotope dosage, the angle formed between the second phase of the tracing and the horizontal, the time required for the curve to reach a peak and the time needed for it to fall from the peak to half that height during the third phase. These data are, however, affected by geometric factors and in many abnormal tracings they are not measurable. Moreover, deductions made from such measurements are often invalidated by the fact that the tracing has been analysed without taking into consideration the relationship between the behaviour of hippuran in the body and the renogram curve. Davies, Jones and Croft (1969), in a renographic study of 20 cases of hydronephrosis before and after pyeloplasty, considered, from inspection of the tracings, that 70 per cent of kidneys showed improvement following operation; of these, 85 per cent improved in tubular function and 50 per cent in emptying. In the present series visual interpretation of the renograms demonstrated undoubted improvement in emptying in 9 of the 32 kidneys after operation but we have been reluctant, for the reasons mentioned above, to make any definite conclusions concerning changes in tubular function.

Analogue computer simulation of pre- and post-operative renograms in our series allowed assessment of alterations in the state of the hydronephrotic kidney in all 32 cases. The renal plasma flow increased significantly after surgery in 8 cases whilst the rate of collection of hippuran increased in 23 instances. That the latter increase was due to improvement in tubular function and not solely to increased renal plasma flow associated with the growth of the child is shown by the fact that commensurate changes did not occur in the contralateral normal kidney.

The most striking post-operative changes in the hydronephrotic kidneys in our series were demonstrated by computer assessment of the emptying rates. Before surgery, kidney emptying was severely delayed in all cases. After operation it was shown to increase in 29 instances. In

6 of these improvement was also evident both from the intravenous urograms and from inspection of the renogram curves; in 8 cases the urogram had improved but the renogram was not obviously changed; in 10 both urography and renography revealed no definite change; in 3 the urograms were unaltered but improvement was apparent from the renograms; in 2 the post-operative urograms appeared worse while the renograms were inconclusive.

Analogue computer assessment of repeated renograms provides a sensitive and convenient method of detecting changes in the state of the individual kidney. The method is, of course, only applicable to the same kidney in the same patient and the interpretation of alterations in renal pathology is facilitated if, as in the present series, the function of the opposite kidney is, and remains, normal. Although we would be loath to make any precise mathematical deductions from the altered rates of collection and evacuation of hippuran by the hydronephrotic kidney after surgery, computer analysis of renograms has shown that significant improvement in tubular function and in emptying rate does occur in most cases even though no definite changes may be detectable on intravenous urography or on simple inspection of renogram tracings.

We are grateful to the Research Committee of the United Liverpool Hospitals and the Liverpool Regional Hospital Board and to the Alder Hey Children's Kidney Fund for the provision of the isotope equipment.

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URETERIC IMPLANTATION IN RENAL TRANSPLANTATION

A Technical Modification

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CADAVERIC renal homotransplantation is now an established surgical procedure. Standard methods for revascularisation of the donor kidney are widely accepted, but the technique of ureteric implantation is not completely satisfactory. The results of several published series have shown a high incidence of ureteric necrosis, leakage, stenosis, reflux and fistula formation. Such complications have led to infection, to loss of the transplanted kidney, and, on occasions, even to a fatal outcome.

Martin *et al.* (1968) in their series of 92 cases had 13 with urinary fistula. Murray *et al.* (1968) reported a 10 per cent incidence of ureteral fistula requiring temporary nephrostomy. The radiological demonstration of these complications was described by Fletcher and Lecky (1969), and their management was reviewed by Williams *et al.* (1970).

Powis *et al.* (1971) in their series of 20 patients who received cadaveric renal transplants had 2 cases of ureteric necrosis. Reflux occurred in 8 out of 18 (44 per cent) of patients with a tunnel implantation and in both their cases without a tunnel. Of the 10 remaining cases 4 had persistent urinary tract infection.

Technique of Ureteric Implantation.—We have used the technique of ureteric implantation involving the fashioning of a sub-mucosal tunnel for the ureter, as described by Politano and Leadbetter (1958) for the correction of vesico-ureteric reflux. Murray and Harrison (1963) first described the use of a tunnel method of ureteric implantation in patients receiving renal transplants.

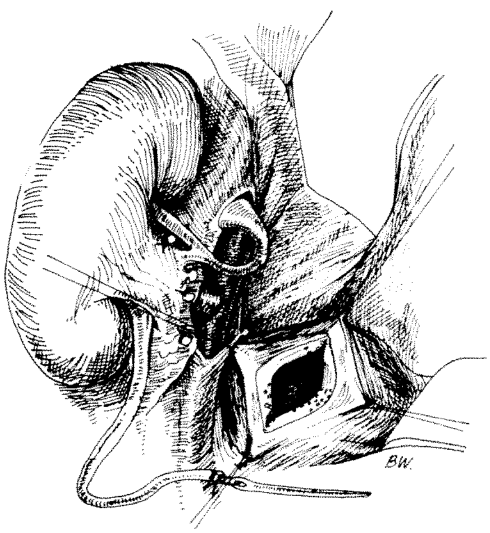

FIG. 1

With this method anterior cystotomy is performed. A submucosal tunnel is created from within the bladder by incising the mucosa in two places and raising it by blunt dissection between them. The ureter is then drawn through the bladder wall and into this tunnel. This technique was used satisfactorily in 24 consecutive cases without complication. However, in some patients the bladder is contracted and the mucosa may be adherent to the underlying muscularis. Attempts to raise it by blunt dissection may result in tearing of the mucosa and a hæmatoma in the tunnel.

For the above mentioned reasons one of the authors (J. S. K.) suggested the following modification. The end of the ureter is attached to the eye of a malleable probe with two loose catgut sutures (Fig. 1). The bladder is mobilised on the side of implantation and an anterior cystotomy is formed. The tip of the probe is then introduced through the muscular layer of the bladder, 3 cm. above the patient's own ureter, until the tip can be seen just beneath the mucosa. The tip of the probe is then gently directed towards the recipient ureteric orifice in the submucosal layer and a tunnel created easily.

This point of entry through the muscular layer and the tunnel is dilated gently with the wider probe.

The bladder mucosa is then incised just above and lateral to the ureteric orifice and the tip of the probe advanced into the bladder cavity (Fig. 2). The probe is gradually introduced into the bladder and then gently drawn through the bladder wall, drawing the donor ureter with it (Fig. 3).

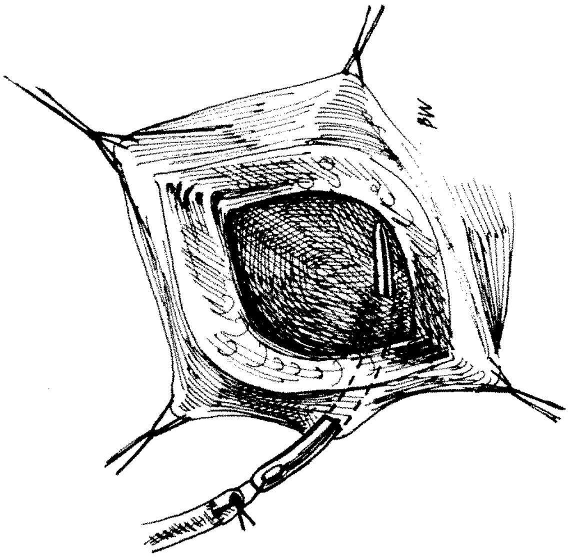

FIG. 2

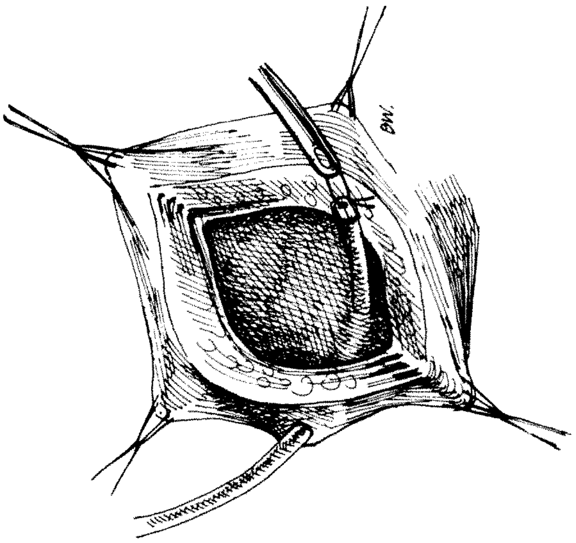

FIG. 3

Using this technique a tunnel of variable length can be easily created and bleeding is minimal. Care is taken to ensure that the ureter is not twisted and lies without tension. The ureter is then anastomosed to the bladder mucosa, using interrupted OOOO chromic catgut, creating a spout or nipple as described by Starzl (1964). The point of entry of the ureter through the muscular layer of the bladder is anchored with one or two catgut sutures. The cystotomy is then closed with 2 layers of continuous O chromic catgut. A self-retaining catheter is inserted into the bladder at the end of operation.

DISCUSSION

In our series of 46 cadaver transplants we have used the technique of ureteric implantation with a submucosal tunnel.

None of these cases has developed an overt complication such as necrosis, urinary leakage or fistula formation. The incidence of stricture and reflux is currently under investigation. We have found that this modification of the technique simplifies the operative procedure.

SUMMARY

This paper presents a modification in the technique of ureteric implantation, which the authors found helpful in their cases of renal transplantation.

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PRESSURE PERFUSION STUDIES OF THE ABNORMAL URETERO-VESICAL JUNCTION

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THIS study was designed to measure the perfusion pressure of abnormal uretero-vesical junctions in vitro, and to ascertain whether an in vitro perfusion study shed any light on the clinico-pathological features of cases where an intravesical or extravesical obstructive element could be present.

Method.—The specimens examined were all operative specimens. The uretero-vesical junction was excised by the standard Leadbetter-Politano (1958) technique, together with as much length of lower ureter as was consistent with satisfactory re-implantation. Great care was taken during the dissection not to interfere with the uretero-vesical junction and the excised segment of ureter more than was necessary. The length of the excised ureteric segment varied from 3 to 6 c. The specimen was immersed immediately in 0·9 per cent saline, and perfused as soon as possible. Repeated perfusion studies undertaken at time intervals of 30 to 60 minutes in three cases showed that there was no significant difference between the pressures obtained after these time intervals and the first perfusion.

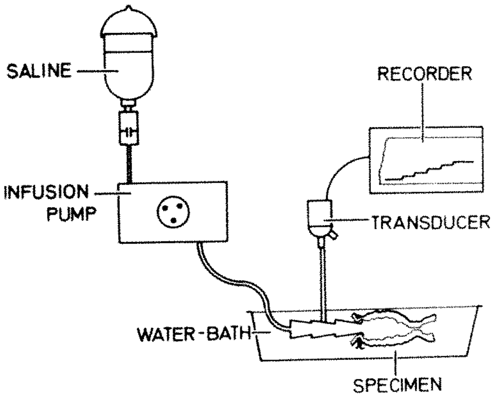

FIG. 1
Pressure recording system.

The proximal end of the ureter was connected to a tap. Proximal to this was a remote-injection catheter, connected at one junction to the outlet tube from the constant pressure/variable rate infusion pump, and at the other end to a physiological pressure transducer, S.E. Laboratories type S.E. 132. The miniature Holter pump, Model R.L. 175, delivered fluid at a rate of 1 ml., 2 ml., 4 ml., 5 ml., 10 ml., 20 ml., 40 ml., and 50 ml. for successive readings, all volumes expresses in ml./minute. The ureteric segment, with its attached manometer lines, was immersed in a bath of 0·9 per cent saline at 37°C. The pressure-recording system is illustrated in Figure 1.

Results.—Eleven cases were studied, and the pressure recordings obtained in these cases are shown in Table I.

It would appear from this Table that the cases could be divided into two groups, a group in which the perfusion pressures were high, and a group in which the perfusion pressures were low.

TABLE I

		Pressure (cm. H_2O)							
		Flow rate (ml./min.)							
Patient	Age (yrs.)	1	2	4	5	10	20	40	50
M. L.	3	1	2	3	3·5	4·5	8	12	14
M. C.	4	0	0·5	1	1·5	1·75	2	3	4
M. F.	10	2	3	0	3	4	9	0	5
L. W.	4	0	0·5	0	2	3	6	6	10
J. S.	6	2	2	2	2	2	4	6	8
K. H.	7	2	3	3	5	9	14	26	28
S. S.	2	20	28	26	30	30	34	38	38
M. T.	30	1	1·5	0	3	4	7	18	36
A. C.	21	8	11	0	18	20	12	0	4
A. P.	6	3	6	7	11	17	23	40	46
P. F.	6	3	2	6	6	6	12	0	16

TABLE II

Relation to Reflux

		Pressure	
	Patient	High	Low
Reflux	M. C.		X
	S. S.	X	
	A. C.	X	
	P. F.	X	
Non-reflux	M. L.		X
	L. W.		X
	M. T.	X	
	A. P.	X	
	P. F.		X
	K. H.	X	
	J. S.		X

For the present discussion we defined a high perfusion pressure segment as one which rose above 15 cm. of water during any of the recordings, and a low pressure segment as one which did not.

The pressures were further related to the presence or absence of reflux, as shown in Table II, and to the ætiological factors as shown in Table III.

On considering the ætiological factors in these cases, we defined the following terms.

1. Primary obstructed mega-ureter, where the ureter is dilated, with no evidence of organic obstruction distally; on calibration it allows easy passage of a bougie; at operation, a definite juxta-vesical obstructed segment is found (Fig. 2).

TABLE III

Aetiological Factors

Patient	Aetiology	Low pressure	High pressure
A. P.	1° obstructed mega-ureter		X
K. H.	1° obstructed mega-ureter		X
A. C.	2° ureteric hydro-ureter (stone and stricture)		X
P. F.	2° ureteric hydro-ureter (diverticulum)		X
M. T.	2° ureteric hydro-ureter (stricture		X
J. S.	2° ureteric hydro-ureter (post-op. stricture)	X	
M. L.	2° urethral hydro-ureter (valves)	X	
M. F.	2° urethral hydro-ureter (valves)	X	
M. C.	Refluxing hydro-ureter		X
S. S.	Refluxing hydro-ureter	X	
C. W.	Idiopathic	X	

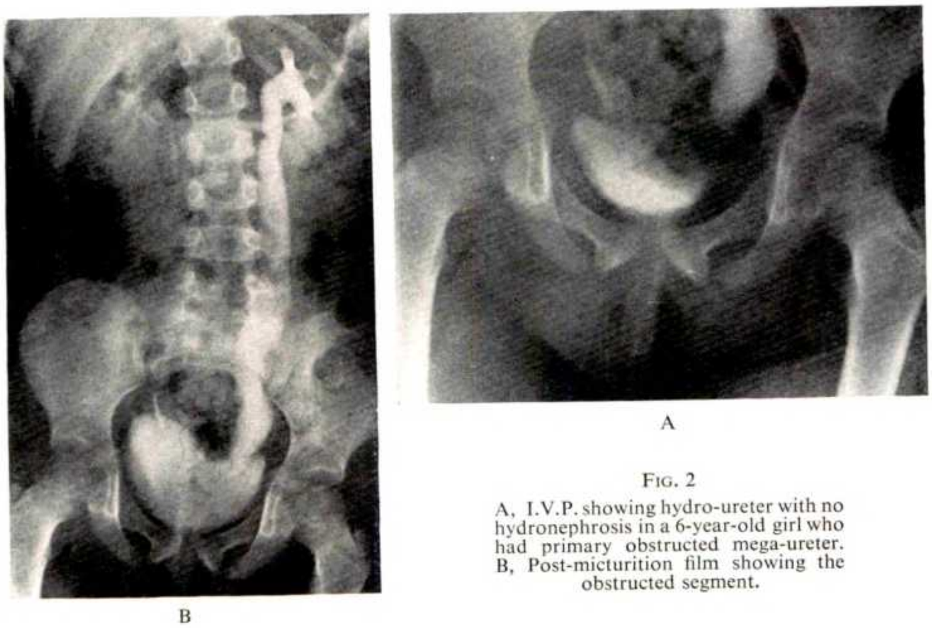

FIG. 2

A, I.V.P. showing hydro-ureter with no hydronephrosis in a 6-year-old girl who had primary obstructed mega-ureter. B, Post-micturition film showing the obstructed segment.

2. Secondary ureteric hydro-ureter, arising as a direct result of intra-ureteric pathology, for example inpacted stone, post-operative stricture, or obstruction due to a para-ureteric vesical diverticulum where there is no evidence of outflow tract obstruction (Fig. 3).

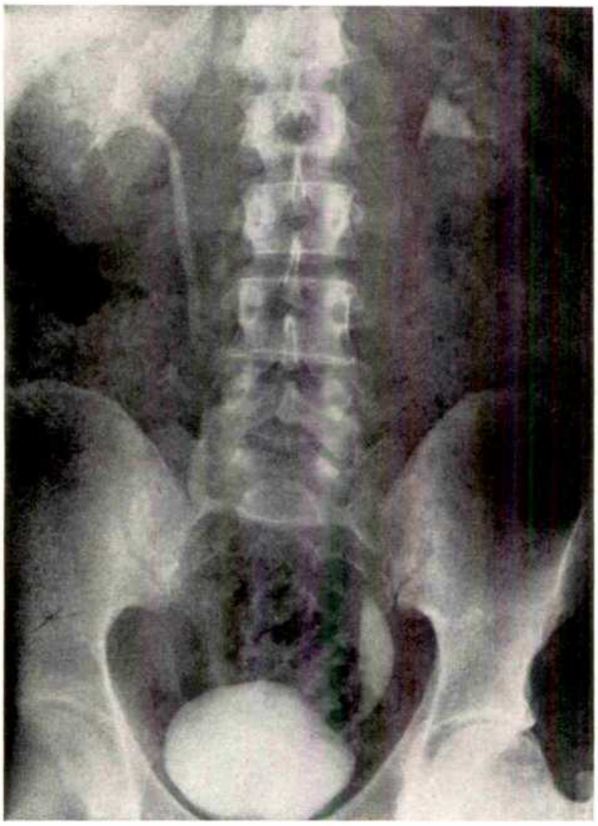

FIG. 3

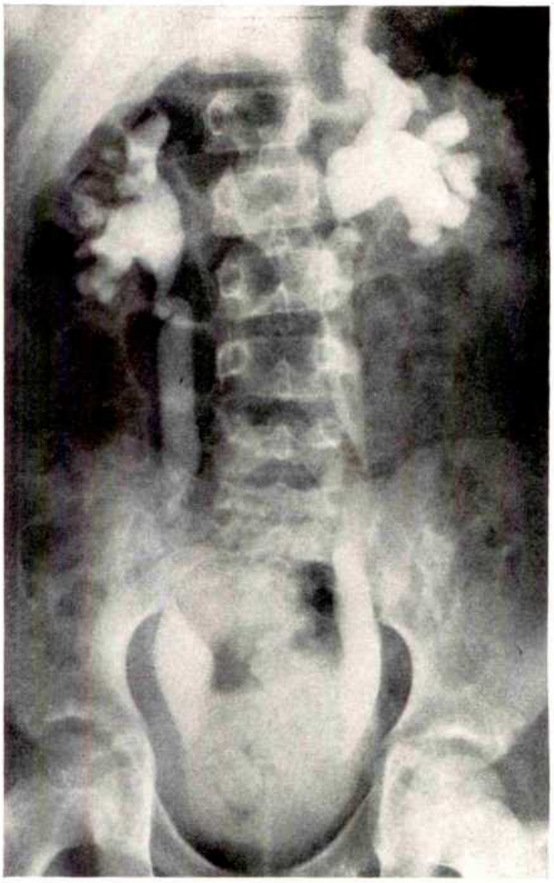

FIG. 4

Fig. 3.—Thirty minute I.V.P. of a 30-year-old man. Note the dilated pelvic spindle. At operation an intramural ureteric stricture was found.

Fig. 4.—(After micturition) I.V.P. film of a 10-year-old boy whose urethral valves were resected at the age of 3 months.

3. Secondary urethral hydro-ureter, where ureteric dilatation is secondary to outflow tract obstruction; in both cases discussed, posterior urethral valves had been resected in infancy (Fig. 4).

4. Refluxing mega-ureter.

5. Idiopathic hydro-ureter, where no ætiological condition could be incriminated.

CONCLUSION

We concluded that there were two types of abnormal uretero-vesical junction, one in which the resistance to ureteric efflux was high, and one in which the resistance was low.

We found that the primary obstructed mega-ureters were of the high pressure type. The secondary ureteric hydro-ureters were usually of the high pressure type (three out of four cases).

Because of the persistence of this high perfusion pressure when the ureter was re-perfused at some time after the excision of the segment, we concluded that the obstruction in these two groups did not appear to depend on neuro-muscular activity. Two current theories concerning the ætiology of the primary obstructed mega-ureter are that the condition is due to either an abnormality of the circular muscle fibres at the lower end of the ureter (Murnaghan, 1957; Tanagho and Smith, 1970), or due to an abnormality of the collagen supporting matrix (Notley, 1971). The activity of the circular muscle fibres would be expected to disappear after some time in vitro, and we would therefore support those workers who suggest that abnormality of the collagen fibres is more important in the ætiology of primary obstructed mega-ureter than abnormal musculature.

In cases of secondary urethral hydro-ureter, we found low pressure curves in the two cases considered. We felt that the ureteric dilatation was secondary to the bladder distension, which is known to occur early in intra-uterine life, and we would compare this condition with the secondary hydro-ureter of adult men, occasionally encountered in cases of benign prostatic enlargement.

We were unable to draw any conclusions concerning the mechanism of refluxing hydro-ureter and idiopathic hydro-ureter, because of the small number of cases falling into these two groups.

SUMMARY

The perfusion pressures of obstructed segments of uretero-vesical junctions have been measured in vitro.

Following analysis of the results obtained it is suggested that the defect in primary obstructed mega-ureter is of the collagen fibres rather than of the ureteric musculature.

It is suggested that secondary urethral hydro-ureter is analogous with secondary hydro-ureter of adult men, seen in some cases of benign prostatic enlargement.

We would like to thank Mr D. Innes Williams for allowing us to study patients under his care, and for encouragement and advice. We are grateful to Mr R. E. Bartholomew, the Institute of Urology, for the photographic illustrations.

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URINARY FISTULA FROM SEGMENTAL INFARCTION IN A TRANSPLANTED KIDNEY: RECOVERY FOLLOWING SURGICAL REPAIR

By M. Fox, M.D., Ch.M., F.R.C.S. and R. C. Tottenham, M.B., B.S.

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A URINARY fistula following renal allotransplantation is a serious complication (Pletka *et al.*, 1969; Starzl *et al.*, 1970). The leakage is usually from the site of the ureteric anastomosis and occurs either early following operation, or a little later, associated with rejection.

An unusual site of leakage is reported in this paper which occurred in the third post-operative month. The site of origin was from a large infarcted section of the kidney following localised arterial spasm during the operation. A method of successful repair is described.

CASE REPORT

The donor kidney was obtained from a healthy 16-year-old male who died following a head injury. The warm ischæmia time was 20 minutes. The left kidney was infused with 250 ml. " Perfudex " followed by fructose (10 per cent) and sodium bicarbonate (1·4 per cent) solutions in equal quantities. Flow and colour changes were noted to be slow, but eventually the kidney became uniformly pale.

The recipient was a 48-year-old female with terminal renal failure from polycystic kidneys. HL-A matching showed identity in 20 specificities tested with 4 positive antigens in each. After uneventful arterial and venous anastomoses to the right iliac vessels (total ischæmic time of 183 minutes), it was noted that while both poles rapidly became pink on release of the vascular clamps the waist region of the kidney remained relatively ischæmic. The arterial supply was re-examined at this stage. The single artery divided after about ¾ cm., into 2 branches. The slightly larger branch supplied mainly the lower pole and the middle part of the kidney, and the smaller branch the upper pole. Pulsation in the lower trunk was reasonable, but its middle and upper main branches were pulsating only feebly. The arterial anastomosis looked normal and there was no thrill.

Azathioprine 1·5 mg. per kg., and Prednisolone 200 mg. reducing to 30 mg. per day over 14 days, were used as immunosuppressive agents. Post-operatively renal function was delayed and a renogram on the 12th day showed poor concentration. Exploration was undertaken on the 14th post-operative day. Both poles of the kidney had a normal appearance and histological examination showed mainly acute tubular necrosis with evidence of some lymphoid infiltration and proliferative vascular changes. The area of relative ischæmia which had been noted initially was found to be infarcted. Steroid dosage was temporarily increased to 200 mg. per day and Actinomycin-C. 200 μg. was given daily for 5 days. Urine output rose gradually from the third week but hæmodialysis was necessary until the 24th post-operative day by which time urine output had reached 2-3 litres per day.

On the 68th post-operative day the patient was re-admitted with a urinary fistula from the wound. Approximately equal amounts of urine were being passed per urethram and from the abdominal opening. The total output, volume and osmolarity remained unchanged, the temperature was normal and the urine was not infected. An excretion urogram showed a normal collecting system without obstruction. A sinogram was not helpful.

Exploration was performed on the 72nd post-operative day. The upper and lower poles of the kidney again looked normal. In the middle of the kidney, running from the hilum laterally across the anterior surface to a point midway on the lateral border, there was a 3-4 cm. band of soft degenerative slough, the remains of the infarcted renal substance (Fig. 1). Urine was leaking from the medial aspect of this area. A ureteric catheter was passed through the opening in the slough and it entered the ureter and bladder without difficulty. A descending ureterogram performed at this stage showed no obstruction at the ureteric orifice.

As preliminary to the repair, the upper and lower poles of the kidney were gently pressed together medially so as to invaginate and enclose the slough between viable renal substance (Fig. 2). This position was maintained by deep 2 " O " plain catgut sutures inserted through the healthy part of the kidney and incorporated into a flap of greater omentum which was brought down from the peritoneal cavity to cover the affected area (Fig. 3). Abdominal wound closure was made leaving a drain, and a self-retaining urethral catheter was introduced into the bladder. The catheter was removed 2 weeks later but re-catheterisation was necessary because of more urinary leakage through the incision. After a further 2 weeks the wound remained dry after removal of the catheter.

The patient remained well during the whole period. The urine however, did become infected with Pseudomonas pyocyanea while the catheter was in place and was controlled by courses of Colomycin and Carbenicillin. It took

4 months to eradicate the infection. Twenty months later her general condition is satisfactory, the urine is uninfected and there has been no deterioration of renal function. Prednisolone 17·5 mg. and Azathioprine 100 mg. daily are being given.

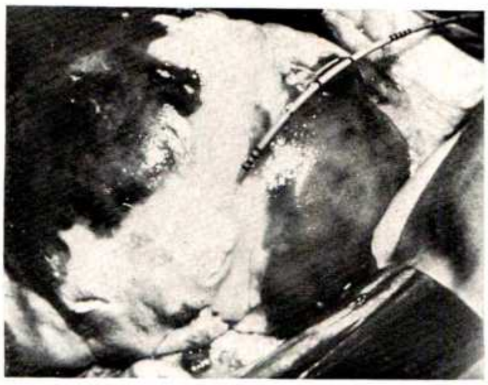

FIG. 1

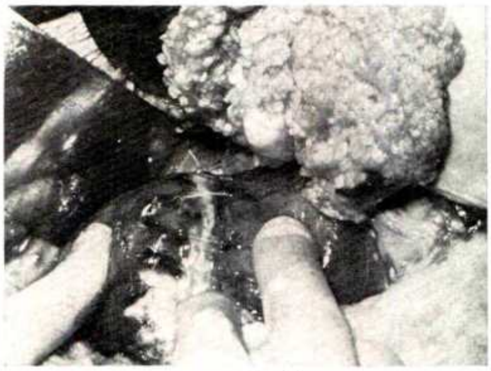

FIG. 2

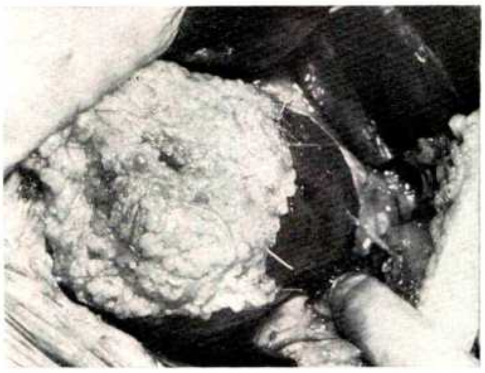

FIG. 3

Fig. 1.—Transplanted kidney showing infarcted area with perforation, through which a ureteric catheter has been inserted.

Fig. 2.—Infarcted area being invaginated by folding of the kidney and by sutures. Flap of greater omentum ready.

Fig. 3.—Suture complete with flap of greater omentum in position.

DISCUSSION

A case of renal allotransplantation is reported in which a late urinary fistula developed postoperatively following infarction of a segment of renal substance. Segmental impairment of blood supply to the kidney first became apparent during perfusion prior to transplantation, excluding renal artery stenosis at the site of the anastomosis as the cause. The kidney was obtained from a young, healthy normotensive subject without arterial disease. Following re-establishment of circulation, return of colour was delayed to the affected segments with subsequent infarction of renal substance.

It has been our impression in the past that slow initial perfusion of the cadaver kidney is associated with a longer period of acute tubular necrosis following transplantation. This is not related to age of the donor. The 2 kidneys in the same subject may perfuse at different rates with varying subsequent periods of acute tubular shutdown. Vascular spasm is probably the major cause. Belzer *et al.* (1970) initially discarded vaso-constricted kidneys for perfusion storage, but subsequently were able to utilise most, following systemic phenoxybenzamine or local procaine infusion—Belzer and Kountz (1970). In the case described in this report the vascular spasm was not treated. It was localised and was followed by both medullary and cortical death in the distribution of supply. Necrosis of renal substance resulted, with a late urinary fistula.

Repair of the leaking infarcted area of the kidney was performed by folding the kidney, invagination of the infarcted substance, suture and the use of a patch of greater omentum to improve blood supply and healing. Infection from a prolonged urinary leak was almost inevitable. It took a long time to clear, presumably because of the large amount of infarcted material present. The patient was fortunate in that the infection was contained and finally eradicated while in the immunosuppressed state.

We wish to thank Mr J. F. V. Larway, for photographic assistance.

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BILATERAL RETROILIAC-ARTERY URETERS

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IN 1960, Corbus, Estrem and Hunt described obstruction caused by abnormal passage of the ureter behind the common iliac artery and vein. A second case was reported in 1969 by Mehl in which the left ureter passed behind the common iliac artery, but anterior to the vein.

The case now described is one of bilateral hydronephrosis with bilateral hydroureters, where each ureter coursed posterior to the common iliac artery and anterior to the vein.

CASE REPORT

T. M., an eight-year-old boy, was born after a full-term, uncomplicated pregnancy and labour. At the age of 2 years he developed right epididymitis and abscess formation which was drained and then healed satisfactorily. He remained asymptomatic until 4 months prior to hospital admission when he had hæmaturia and was subsequently found to have urinary infection. The infection responded to a 10-days' course of Trimethoprem. He passed urine rather infrequently, and was incontinent from time to time.

On examination, he was an undersized boy who weighed 19·6 kgm. His blood pressure was 120/65 and his temperature 98·2° F. The bladder was palpable, 3 fingers above the pubic crest, and the right testicle was atrophic with a scrotal scar above it. His hæmoglobin was 13·2 mg. per cent; blood urea 60 mg. per cent; creatinine 1·3 mg per cent; sodium 141 mEq./l.; potassium 3·9 mEq./l. and CO_2 21 mEq./l. His urine on admission was sterile. An intravenous pyelogram showed gross bilateral hydronephrosis in a horseshoe kidney and bilateral hydroureters (Fig. 1).

Bilateral nephrostomy was performed on 9th July 1970. Following this his general condition improved and his blood urea fell to 35 mg. per cent. Three weeks later a bilateral nephrostogram was performed. The contrast injected through the drainage tubes outlined grossly dilated ureters, each narrowed at a point below the pelvic brim (Fig. 2). Both ureters showed poor peristalsis.

Micturating cystourethrogram revealed bilateral vesico-ureteric reflux: on the left, this extended up to a point corresponding to the narrowed ureteric segment seen in the intravenous pyelogram; on the right side the reflux was more free, but still showing a similar ureteric narrowing (Fig. 3). There was also reflux into a third tube which appeared to enter the bladder at the posterior midline of the bladder neck and curved laterally towards the right inguinal opening (Fig. 4). He emptied his bladder completely with no evidence of outlet obstruction. The bladder refilled with the refluxed dye.

Exploration of the lower abdomen through a Pfannensteil incision was performed on 4th August 1970. Both ureters coursed behind the common iliac arteries and were grossly dilated above the vessels, less so below. The third tube was found to be an enormously dilated right vas deferens which had taken the appearance of a ureter. It had a fistulous opening into the posterior midline of the bladder and was followed laterally to the internal inguinal ring. The left vas deferens appeared to be thickened. The bladder wall was slightly hypertrophied. The dilated right vas was excised. The ureters were mobilised, cut across and brought anteriorly to the iliac arteries. The distal 5 centimetres was excised. The ureters were remodelled over a 10 F.G. portex tube and re-implanted into the bladder through submucosal tunnels. A 14 F.G. Malecot catheter was inserted in the bladder, the portex tubes left as ureteric splints and the retropubic space drained. The wound was closed in layers. He made an uneventful recovery. The drain was removed after 48 hours, the ureteric splints removed on the 10th post-operative day and the Malecot catheter 2 days later. Finally, the nephrostomy tubes were removed 2 days later. He was discharged home with sterile urine and kept on Gantrisin, 0·5 G., b.d.

The resected portion of the third tube was 8 cm. long with an external diameter of 1·2 cm. at one end and 0·4 cm. at the other.

On histological examination it had the appearance of a ureter, the wall of which was thickened due to muscular hypertrophy and fibrosis. The lining epithelium was transitional in type and the lamina propria was infiltrated with chronic inflammatory cells (Fig. 5).

He remained symptom free, dry day and night, with sterile urine, and was re-admitted three months later for follow-up investigations. An intravenous pyelogram showed poor excretion of the dye, particularly on the right side, and the dilatation of the pyelocalyceal system and upper ureteric segment remained (Fig. 6). A cystogram showed that the vesico-ureteric reflux persisted on the right side (Fig. 7). The blood chemistry was urea 32 mg. per cent and creatinine 1·0 mg. per cent.

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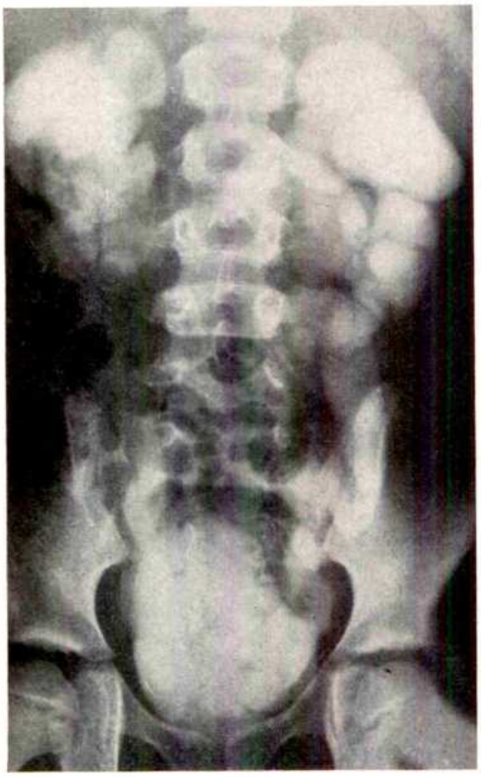

FIG. 1

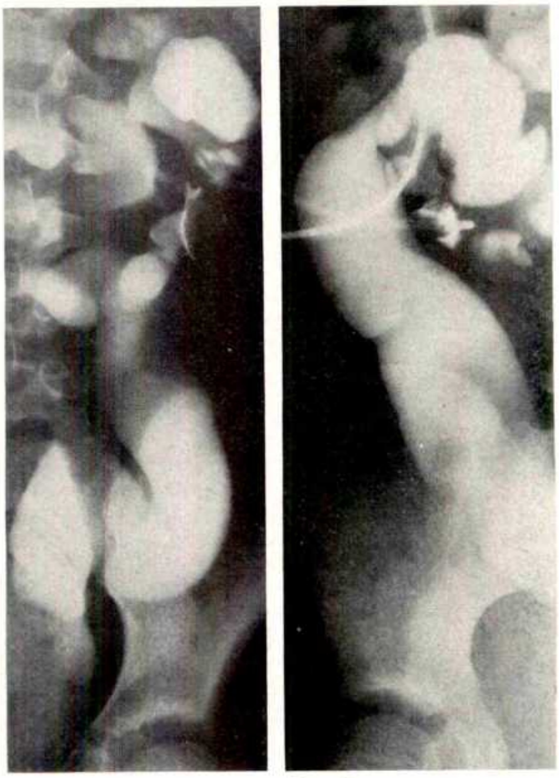

FIG. 2

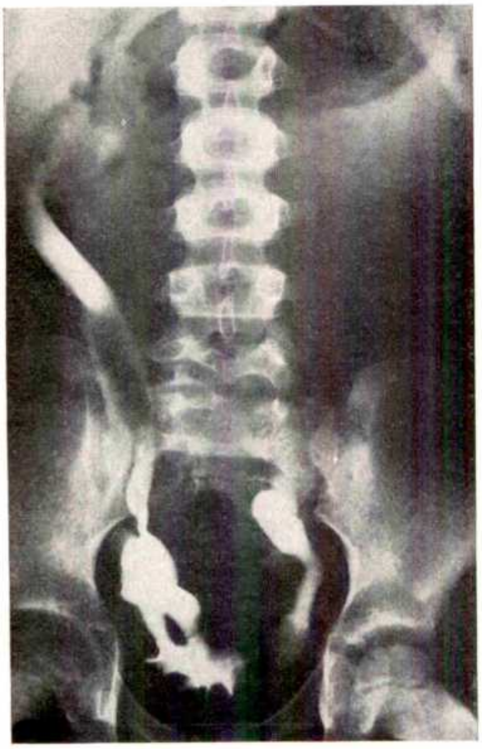

FIG. 3

Fig. 1.—Intravenous pyelogram. Bilateral hydronephrosis, hydroureters.

Fig. 2.—Nephrostogram showing dilatation of ureters down to where compressed by common iliac arteries.

Fig. 3.—Micturating cystourethrogram showing reflux into three tubes; on the left up to the point of obstruction.

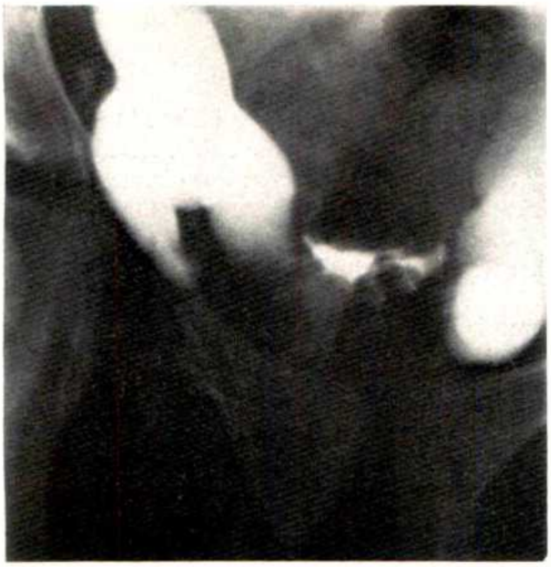

FIG. 4

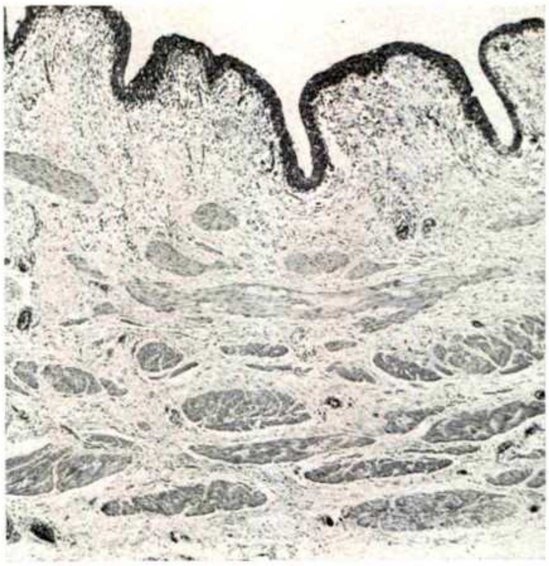

FIG. 5

Fig. 4.—Micturating cystogram showing the direction of the dilated third tube (vas) towards the inguinal ring.

Fig. 5.—Transverse section through the dilated segment of the right vas showing its ureterisation. Note the transitional cell epithelium.

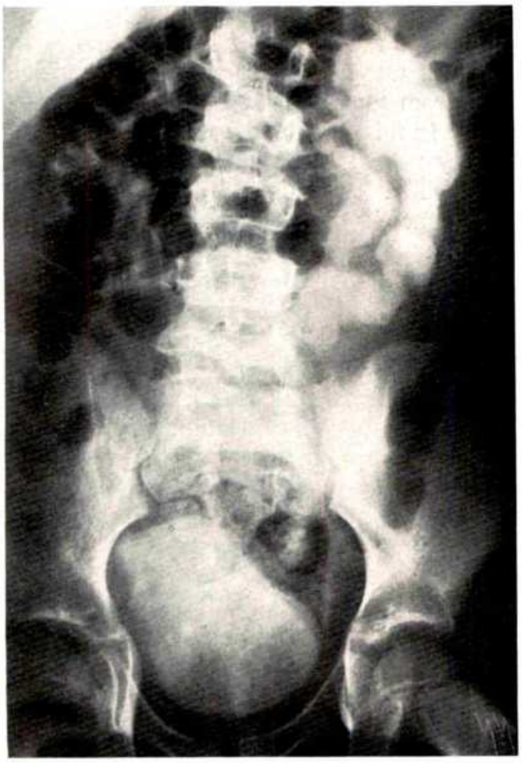

FIG. 6

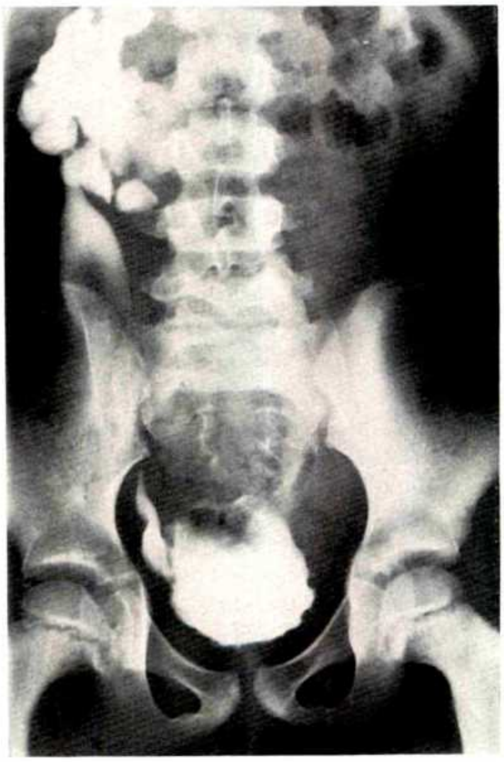

FIG. 7

Fig. 6.—Post-operative intravenous pyelogram. Poor excretion of the dye, more marked on the right side.

Fig. 7.—Post-operative micturating cystogram showing free vesico-ureteric reflux up to the dilated right kidney and upper ureter.

DISCUSSION

Retroiliac ureter is an extremely rare abnormality. This case reported is believed to be the third in literature. The salient features of these cases are summarised in the Table. In all three cases no pre-operative diagnosis of the abnormality was made and treatment was directed to the ureter rather than to the vessels. Our patient differed from the other 2 cases in that (*a*) the anomaly was bilateral, and (*b*) there was ureteric dilatation distal to the vascular obstruction, probably due to vesico-ureteric reflux, which together with the gross ureteric dilatation proximal to the artery, influence the treatment.

Division of the inferior vena cava and reanastomosis for retrocaval ureter was recommended by Cathro (1952) in cases where the opposite kidney function is severely impaired or is absent. Goodwin *et al.* (1957) reviewed the literature on retrocaval ureter cases and discussed the treatment. They interviewed 37 urologists, some of whom would have divided the ureter, while others preferred to sever the vena cava. On this basis Mehl (1969) questioned whether it would have been better to transect and reanastomose the iliac artery rather than the ureter. In his patient the kidney was grossly hydronephrotic and the contralateral kidney was absent.

In our patient both ureters were grossly dilated above and, to a lesser extent, below the vessels. In addition to the resiting, the calibre of the ureters was reduced in order to achieve better peristalsis. However, we failed to correct reflux on one side, probably due to the poor quality of the ureteric musculature, *i.e.* poor peristalsis. Perhaps temporary cutaneous ureterostomies would have allowed more functional recovery of the ureters, should this occur. It was conceivable that the ureteric segment behind the vessel was not quite normal as it had been compressed by a major vessel since intra-uterine life.

The history of epididymitis, abscess formation and the radiological evidence of reflux into a third tube of peculiar course suggested that its nature was a vas deferens. The occasional enuresis was probably due to regurgitation of urine from the vas into the posterior urethra. Epididymitis is known to be a rare disease in children. In this case there was no radiological or cystoscopic evidence of outflow obstruction, nor any neurological abnormality. The right ureter was followed at operation and found to open normally. It did not join the vas. The cause of urinary reflux into the dilated vas was not clear, but once its course at operation was verified there was no hesitation in excising the dilated segment and tying off its upper end. This was because such a dilated tube was unlikely to be a satisfactory conduit for spermatozoa and if left behind recurrent epididymitis might have occurred (Williams and Royle, 1969).

With the appearance of the ureteric bud the terminal part of the nephric duct (Wolfian duct) between the bud and the cloaca is known as the common duct. By the 14-15 mm. stage, the common duct is fully absorbed. The ureter and Wolfian duct open independently into the urogenital sinus and, as the ureteric bud elongates, its relation to the nephric duct changes. The precise nature of the factors of growth and differentiation resident in the nephric duct and ureteric bud are not fully understood (Mehta, 1967). It seems justifiable, therefore, to assume the presence of growth factors plus a few key substances (inductors) and secondary operative physico-mechanical local factors (Mehta, 1967). There is good evidence that the nephric duct (the future vas deferens) is the inductor of integrated urogenital development. The absence or destruction of the duct yields widespread anomalies, not only of the structures directly developing from it, but also of structures induced by it, such as ureter and kidney.

In our patient the right vas proved histologically to be abnormal and the left vas appeared to be macroscopically abnormal. Whether the abnormal vasa deferentia in our case induced urinary tract abnormality, or the dilatation of the right vas was due to urinary reflux resulting in transformation of the non-ciliated columnar epithelial lining into transitional cell epithelium, is a matter for speculation.

Table

Summary of reported cases of Retroiliac Ureters

	Sex	Age	Site	Presentation	Nature of Abnormality	Ureter distal to Vascular Obstruction	Associated Abnormalities	Treatment
Case 1. Corbus *et al.*, 1960	F	25	Rt.	Recurrent urinary infection and hæmaturia	Right ureter courses posterior to artery and vein	Normal calibre	Left kidney normal. No associated abnormality	Division of the ureter obliquely and reanastomosis over a splint anterior to the vessels
Case 2. Mehl, 1969	F	15	Lt.	Recurrent urinary infection	Left ureter courses posterior to artery, anterior to vein	Normal calibre	Imperforate anus and recto-vaginal fistula. Œsophageal atresia and tracho-œsophageal fistula. High bifurcation of ærta. Absent left internal iliac artery. Absent right kidney	Division of ureter transversely and reanastomosis anterior to the artery
Case 3	M	8	Bil.	Hæmaturia and urinary infection	Both ureters posterior to the artery and anterior to the vein	Dilated	Horse-shoe kidney. Reflux into right vas	Bilateral nephrostomy. Division of ureters. Tapering and reimplantation in the bladder

Follow-up: *Case 1.* Asymptomatic, urine sterile, follow-up pyelogram of doubtful value because of two consecutive and uneventful pregnancies.

Case 2. Patient is symptom free, urine sterile, blood fell from 230 mg. per cent to 70 mg. per cent. However, the patient went into renal failure necessitating regular hæmodialysis. She was given a cadaver kidney homotransplant which is functioning satisfactorily.

Case 3. Poor excretion of dye, more so on the right side. Upper tract dilatation and upper ureteric dilatation remains. Failure to prevent vesico-ureteric reflux on the right side. However, the blood chemistry is satisfactory.

SUMMARY

A case of bilateral retroiliac ureters of a horseshoe kidney and urinary reflux into a dilated ureterised vas deferens is reported.

Two previously reported cases of retroiliac abnormality are reviewed and the method of treatment is discussed.

I would like to express my thanks to Mr D. Innes Williams for allowing me to report on this patient.

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INTESTINAL CONDUIT URINARY DIVERSION IN CHILDREN

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SHOEMAKER (1960) is credited with the first description of urinary diversion by ileal conduit. However, it was Bricker (1950) who popularised it in recent times. The demonstration that the unusually high incidence of hyperchloremic acidosis (81 per cent according to Ferris and Odel, 1950) can be eliminated by conversion of ureterocolic anastomosis to uretero-ileo cutaneous anastomosis (Persky, 1958), established the latter as the choice procedure for surprapubic urinary diversion for benign as well as malignant conditions. We, herewith, present our experience with intestinal conduit urinary diversion at the Montreal Children's Hospital.

Material and Indications.—Sixty-six children who had intestinal conduit urinary diversion (62 ileal and 4 sigmoid conduits) at the Montreal Children's Hospital between 1956 and 1970 are reviewed. Thirty-seven patients were male and 29 female. The age at the time of diversion ranged from 6 months to 18 years. Fourteen were less than 4 years of age, while 32 patients were 5 to 9 years old, and 20 patients were 10 years or older (Table I). In 21 patients other types of urinary diversions were performed prior to conduit formation (Table II). Patients with less than 1 year follow-up were excluded. The follow-up period varied from 1 year to 9½ years (average 3½ years). All patients were followed in the special " Ileal Bladder " Clinic every six months utilising a variety of investigations including intravenous pyelogram, cine pyelogram, ileogram, urine culture, BUN, creatinine and electrolyte determination. Urine specimens for culture were obtained by passing a sterile catheter into the segment. Stomas were inspected and problems

TABLE I

Total Number of Patients	66
Male	37
Female	29
Age at Operation (6 months to 18 years)	
0-4 years	14
5-9 years	32
10 years and over	20

TABLE II

Types of Urinary Diversion performed prior to Ileal Conduit

Cystostomy	15
Cordonnier type vesico-ileo-cutaneous anastomosis	1
Uretero-sigmoid anastomoiss	1
Nephrostomy	4
Total	21

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related to the appliances were discussed and solved with the assistance of an experienced stomatherapist.

The most frequent indication for diversion was neurogenic vesical dysfunction due to meningomyelocele. The other indications are listed in Table III.

TABLE III

Indications for Urinary Diversion

Neurogenic (Total 33)	
Meningomyelocele and sacral agenesis	27
Spinal trauma	3
Spinal tumour: Ependymoma 1 Hemangioma 1 Sacral teratoma 1	3
Congenital (Total 25)	
Bladder neck obstruction	8
Urethral valve	7
Exstrophy	9
Urethral stricture	1
Reflux (Total 7)	
Neoplastic (Total 1)	
Rhabdomyosarcoma of prostate (total cysto-prostatectomy)	1

Results.—There were 5 deaths among the 66 patients. The causes of death are documented in Table IV. The status of the upper tract before and after operation is listed in Table V. The upper tract units were classified as normal, mildly to moderately dilated and moderately to severely dilated by the degree of dilatation in the ureters and pelvi-calyceal system.

TABLE IV

Mortality

Number of Deaths—5

Post-op	Cause of Death
4 months	aerobacter septicaemia collapse, multiple abscesses in kidney
6 months	brain tumour at cerebello-pontine angle-detected at autopsy
6 months	pulmonary metastases from sarcoma of prostate
4 years	retroperitoneal abscess
9½ years	intracranial hæmorrhage, renal failure, hypertension

Eighty-two per cent of the patients had infected urine pre-operatively and 52 per cent continued to remain infected after operation. The overall deterioration in BUN and creatinine in all patients in the post-operative period was 30·3 per cent. However, of the patients who were operated with a high pre-operative value of BUN and creatinine, 50 per cent showed deterioration in the biochemical determinants after surgery (Table VI).

TABLE V

Intravenous Pyelograms

Pre-op	Number	Post-operative Improved	Post-operative No change	Post-operative Worse
Normal	31	—	21	10 (32%)
Minimally or Mildly obstructed	29	10 (34%)	12 (41%)	7 (24%)
Moderately to Severely obstructed	54	23 (42·5%)	11 (20%)	20 (37%)
Totals	14	33	44	37 (32·4%)

TABLE VI

Biochemistry

		Post-operative Values No change	Post-operative Values Improved	Post-operative Values Worse
Patients with normal pre-op values	38	32 (84·3%)	—	6 (15·7)%
Patients with high pre-op values	28	2 (7·2%)	12 (48·8%)	14 (50%)
Total	66	34 (51·5%)	12 (18·1%)	20 (30·3%)

Complications.—The early and the late complications are tabulated in Table VII. Abdominal distension in the immediate post-operative period was universal despite continuous gastric suction and intravenous fluid therapy. One patient was anuric in the first 48 hours. Wound dehiscence occurred in 1 patient. These patients all had evidence of azotemia in the pre-operative period. One patient developed a hernia of small bowel through the ileostomy opening requiring operative correction, and another had ileocutaneous fistula which cleared up spontaneously. Osteodystrophy occurred in 5 patients as a late complication and uretero-ileal anastomosis obstruction was encountered in 8 patients. The metabolic acidosis in 5 patients was sufficient to require maintenance therapy with sodium bicarbonate. Post-operatively renal calculi occurred in 5 patients despite apparently non-obstructed drainage tracts on pyelography. Three of these had gross hydronephrosis and hydroureter before operation.

DISCUSSION

Ileal urinary diversion sacrifices continence to achieve effective urinary drainage with minimal resistance to flow. The isolated bowel segment provides the double advantage of constant

TABLE VII

Complications

Early	
Pneumothorax	1
Convulsions	1
Abdominal distension	10
Ileo-cutaneous fistula	1
Staph. abscess	1
Anuria	1
Retroperitoneal abscess	1
Hernia of small bowel through ileostomy opening	1
Pyelonephritis	
Wound dehiscence	1
Bowel obstruction	2
Late	
Stoma	36
Osteodystrophy	5
Metabolic acidosis	5
Uretero-ileal junction stenosis	8
Renal stone	5

peristalsis and isolation from fecal stream, thereby, minimising electrolyte disturbance and ascending infection. The results are compared with reports from other centres.

Upper Tracts.—One hundred and fourteen upper urinary tract units were available for follow-up. Thirty-three were normal, 29 minimally to moderately dilated and 54 moderately to severely dilated during the pre-operative period as judged by pre-operative intravenous pyelogram. Forty-two per cent of the severe hydronephrosis group improved in the post-operative period. King and Scott (1962) found that patients with normal or near normal intravenous pyelograms continued to show normal pyelograms whereas, patients with moderate to severe hydronephrosis failed to improve or showed progressive dilatations. This has not been our experience. Thirty-two per cent of our normal pre-operative pyelograms deteriorated during the post-operative period. The incidence of similar deterioration in the other series has been variable. Susset (1966) reported a 42 per cent incidence, Cook, a 29 per cent incidence, Retik (1967), a 15 per cent incidence, and in Straffon's series, it was 11 per cent. Our results compare well with those of Cook (1968). In most of these cases the cause of dilatation has not been determined. Uretero-ileal obstruction, stomal obstruction, increased intraluminal pressure, infection, reflux—have all been suggested as possible explanations.

An increased mortality rate has been noted when diversion is carried out in the presence of severely compromised renal function (Rickham, 1964). In these cases it is justifiable to do a temporary diversion such as a nephrostomy or a ureterostomy to promote stabilisation of the upper urinary tract and improve renal function prior to a definitive diversion. A retrospective analysis suggested a tendency to delay urinary diversion in our earlier cases. An earlier diversion may conceivably have reduced the incidence of a large number of pre-operative dilated units.

The present series demonstrates a 33 per cent deterioration which correlated with the 30 per cent incidence of deterioration noted in the biochemical parameters.

Bladder Status.—Stagnant cystitis occurred in 12 per cent of the patients and, while mostly insignificant, 1 patient required cystectomy. Cook has reported an incidence of 25 per cent, all clearing with hibitane irrigation. In Retik's series, 10 of the 85 children required cystectomy for persistent vesical infection. The patient in our series who required cystectomy had concomitant outlet obstruction following previous bladder neck surgery.

Stomal Complications (Table VIII).—Thirty-six of 66 patients had some form of stomal complication—ulceration, dermatitis, acanthosis, encrustation of salt, recession, prolapse, hæmorrhage, partial sloughing; stenosis and formation of ileo-cutaneous fistula have been encountered. Twenty-seven patients (40 per cent) needed at least 1 revision of the stoma and 6 patients required up to three revisions. In Cook's series, 15·7 needed stomal revision, whereas, in Retik's series, 24 per cent required revision. In our series the majority of the complications, either minor, giving rise to patient annoyances, or major, leading to clinically significant sequelae, have been related to the stoma or the appliance. Stomal stenosis can occur at any level between skin and peritoneum. Since children with neurogenic dysfunction frequently have associated orthopædic deformity of the spine and pelvis, special care should be taken in planning the stoma site. The appliance is fitted pre-operatively with the patient sitting up to ensure that hip flexion does not displace the flange. Proper fitting of collective device is important. Improper fitting, the removal of the plastic ring without dissolving cement leading to avulsion of the epidermis, a small appliance leading to constant bathing of the stoma with urine, with phosphate deposition, too large an aperture that allows constant bathing of the skin around stoma with urine leading to pseudo-epitheliomatous hyperplasia, and red, raw skin-wound all eventually lead to stenosis at skin level. Stomal stenosis refractory to conservative treatment should be revised.

TABLE VIII

Complications

Stoma (Total 36)	
Ulceration	
Dermatitis, acanthosis	
Encrustation of salt	
Recession	
Prolapse	
Hæmorrhage	
Partial sloughing	
Stenosis	
Stomal Stenosis (Total 27 pts—40%)	
Total number of revisions	40
Patient needing 3 revisions	6

SUMMARY

A review of 66 intestinal conduit urinary diversions (62 ileal and 4 sigmoid conduits) done between 1956 and 1969 at the Montreal Children's Hospital is presented. Twenty-one of these patients underwent other types of diversions prior to conduit formation. The most frequent indication for diversion has been neurogenic vesical dysfunction due to meningomyelocele followed by other congenital anomalies. There was an overall deterioration of 30 per cent of all upper tracts. When broken down, it was seen that 32 per cent of normal pre-operative pyelograms deteriorated in the post-operative period, whereas, 42 per cent of the severely hydronephrotic group improved after operation. The most frequent morbidity was associated with the ileostomy stoma and its appliances. Forty per cent of patients in our series needed at least one revision of stoma. Intestinal conduit operations are associated with a significant morbidity and require great care in planning the surgery, as well as careful long-term follow-up in the post-operative period.

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PHEOCHROMOCYTOMA OF THE URINARY BLADDER

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PHEOCHROMOCYTOMA, a tumour arising from the chromaffin tissue, originates most commonly in the adrenal medulla. Approximately 40 per cent of these tumours are observed in extra-adrenal sites (Page and Copeland, 1968). The following case of pheochromocytoma of the urinary bladder is reported because of its rarity.

CASE REPORT

A 65-year-old Hindu woman was seen for her complaint of hæmaturia. Hæmaturia was total, profuse and lasted for 2 days. It was not associated with any other urological symptom. She gave history of a similar attack of hæmaturia lasting for a day, 2 months prior to the date of examination. The past urological history was negative and she had never suffered from hypertension. The physical examination was essentially negative. Her B.P. on admission was 130/70 mm. of Hg. Urine analysis revealed frank hæmaturia with very few W.B.C.s. An intravenous cystogram revealed a filling defect in the left wall of the bladder (Fig. 1). A cystoscopic examination revealed a solid pedunculated tumour situated on the posterior wall of the bladder wall. Dilated blood vessels were seen over the surface of the tumour which was smooth. The rest of the bladder was essentially normal. A biopsy of the tumour was performed. The bi-manual examination suggested a solid lesion with no extra vesical extension. The histopathology of the biopsy material suggested a possibility of a pheochromocytoma. The blood pressure of the patient was noted repeatedly at different times of the day and night as also before and after micturition. The blood pressure continued to remain within normal range. The estimation of 24-hour urinary excretion of catacholamines was 145 mg. Vanil Mandelic Acid Tests showed 4·8 mg. of VMA per 24-hour urine. The patient was subsequently operated upon and a partial cystectomy was performed by a combined transvesical and extravesical, extraperitoneal approach. Immediately after the induction of anæsthesia the blood pressure rose to 220/120 mm. of Hg. It settled down to 160/110 mm. of Hg within 10 minutes. When the tumour was handled during its removal, blood pressure again rose to 220/115 mm. of Hg and as soon as the tumour was removed the blood pressure dropped to 100/60 mm. of Hg in spite of the fact that blood loss was negligible. 700 ml. of blood was transfused rapidly. It restored the blood pressure to 130/80 mm. of Hg after which the B.P. and pulse remained steady till the end of operation. The details of the anæsthestic management of the case are being reported elsewhere. Subsequent post-operative convalescence of the patient was uneventful. The histopathology of the specimen and the hormonal estimations of the tumour tissue confirmed the diagnosis of pheochromocytoma of the urinary bladder.

The catecholamine content per gram of tumour tissue was estimated by fluorimetric method—(Sobel and Henry, 1957). Total catecholamine content was 3·75 mg./gm. of tumour tissue. (In pheochromocytoma the catecholamine content varies from 0·7 mg. to 9·7 mg./gm. of tumour tissue (U. S. Von Euler, 1958).)

Pathologic Features

Gross Observations.—Specimen received in the laboratory consisted of a portion of the urinary bladder measuring 4·5 × 4 × 2 cm. It showed a soft polypoid mass projecting from the mucosal surface measuring 2·5 × 1·5 cm. in size. It presented a pale reddish-brown appearance. On cutting, the tumour was seen to extend into the muscle coat in the form of a soft lobulated mass with a glistening hæmorrhagic surface. After a few hours fixation in formalin, the tumour acquired a deep brownish-black appearance (Fig. 2).

Microscopic Findings.—The main bulk of the tumour was situated in the muscle coat extending through the full thickness of the wall whereas the rest of it was projecting as a polypoid mass on the mucosal surface (Fig. 3).

The tumour was composed of ovoid, polygonal or fusiform cells with indistinct outlines, the cytoplasm of the adjoining cells merging with one another. The cytoplasm was abundant, slightly basophilic and exhibited a striking, fine granularity. At places the cells showed a foamy or vacuolated cytoplasm (Fig. 4). Nuclei were rounded, eccentrically situated and showed a

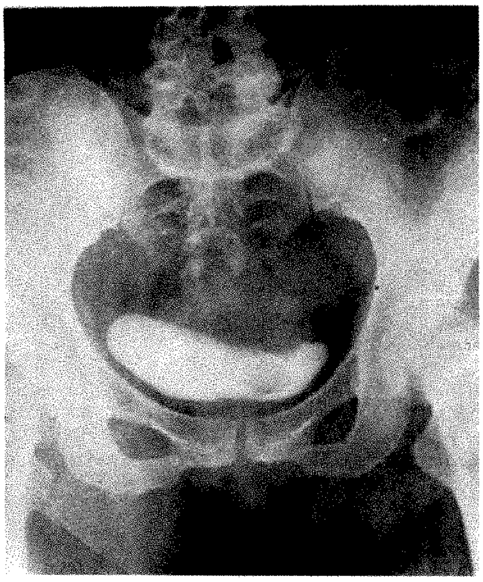

FIG. 1

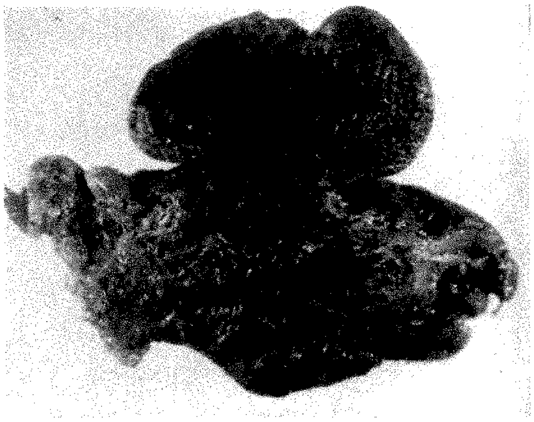

FIG. 2

Fig. 1.—I.V. Cystogram 30 minutes after injection shows an ovoid filling defect in the left side of the bladder.

Fig. 2.—Gross appearance of the bisected tumour a few hours after formalin fixation. The tumour has considerably darkened in colour.

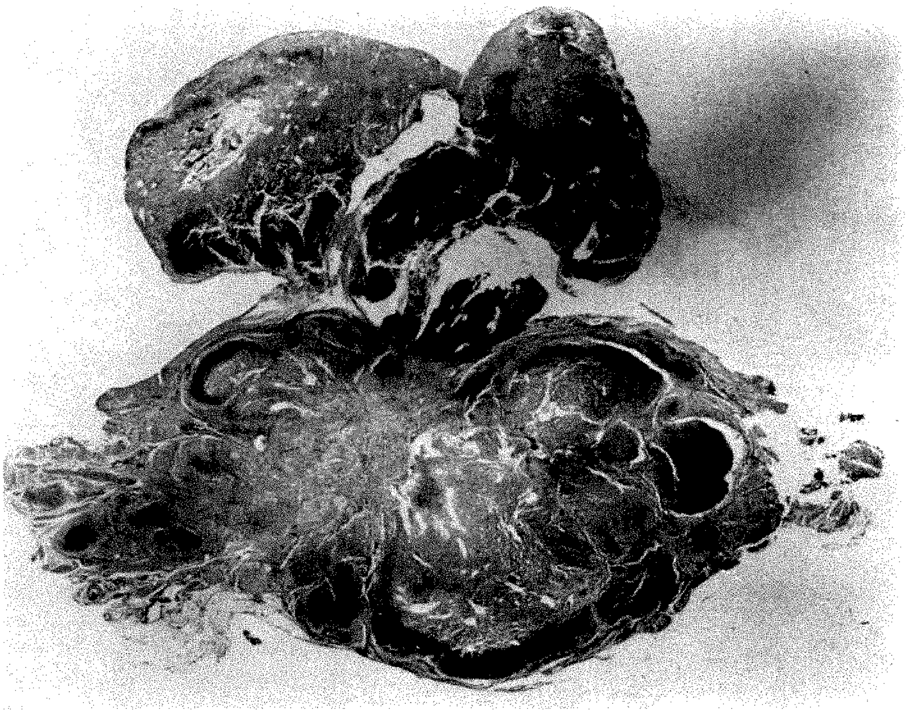

FIG. 3

Photomicrograph of the entire tumour—note the irregular extension of the tumour through the muscle bundles. (H. & E. ×4).

scattered chromatin. There was a moderate variation in the size of the nuclei. Mitotic figures were rarely observed. Stroma consisted of thin strands of connective tissue separating the tumour cells into alveolar groups or lobules of irregular sizes and shapes. The tumour was extremely vascular showing a number of blood capillaries ramifying between the neoplastic cells.

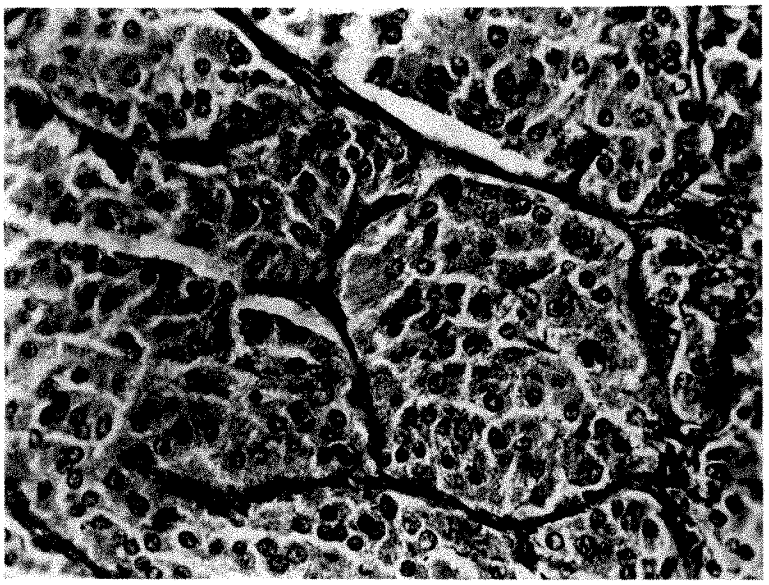

FIG. 4
High power view of the tumour cells—the cytoplasm is granular. Nuclei are rounded and uniform (H. & E. ×280)

The tumour was intimately related to the muscle coat. Groups of tumour cells were extending in between the muscle bundles giving an appearance of infiltration. The transitional epithelium overlying the tumour was separated from the tumour by an œdematous submucosa. Areas of hæmorrhage were seen particularly in the polypoid portion of the tumour.

DISCUSSION

Pheochromocytoma, primarily involving the urinary bladder, is of extremely rare occurrence. As suggested by Zimmerman *et al.* (1953) and Scott and Eversole (1960) the tumours arise from the paraganglia related to the autonomic nerves of the urinary bladder. Since the first case published by Zimmerman *et al.* in 1953, 30 cases of primary pheochromocytoma of the urinary bladder have been recorded in the world literature. Out of these 30 cases, 24 have been documented in the paper published by Albores-Saavedra *et al.* (1969). The other 6 cases of primary pheochromocytoma of the bladder recorded in the literature are by Lumb and Gresham (1958), Derome *et al.* (1960), Silver (1960), Milliez *et al.* (1963), Withycombe (1965) and Bourne and Beltaos (1967).

Pheochromocytoma of the urinary bladder produces a peculiar symptom complex owing to its location in the structure which constantly changes its dimensions during the filling and emptying processes. A combination of episodes of hypertension during or immediately after micturition associated with hæmaturia are almost pathognomonic of pheochromocytoma of the urinary bladder. In more than 50 per cent of patients episodes of hypertension consisting of throbbing headache, palpitation, profuse sweating occur. Painless hæmaturia is also observed in about half the patients. Clinical diagnosis is easily arrived at if the patient presents with the entire syndrome. However, if only the hypertensive episodes due to secretion of catecholamines are produced, a prolonged search may be required before a primary pheochromocytoma in the bladder may be located. On the other hand, if the bladder symptoms are predominant in the absence of hypertension, it may be extremely difficult to arrive at a correct diagnosis as happened in the present case. The only presenting symptoms in the present case were episodes of sudden painless hæmaturia. Even on careful inquiry the patient denied hypertensive episodes during or after micturition. Values of blood pressure recording were within normal limits.

The real nature of the lesion was suspected only after the biopsy examination. Pheochromocytoma of the urinary bladder without associated hypertension is rarely encountered, being observed in only 2 of the 27 cases published so far (Blair and Brandwood, 1963; Pugh *et al.*, 1960).

The variation in the symptom complex are partly due to the location of the tumour in the bladder wall. If close to the mucosal surface it commonly gives rise to hæmaturia. In the present case, although the main bulk of the tumour was deep in the muscle coat, a large portion was projecting as a polypoid mass into the lumen. The tumours restricted within the wall of the bladder or extending towards the serosal aspect are usually silent as far as urinary symptoms are concerned.

In retrospect there was no clinical feature in this case that could have raised a suspicion of such a lesion. The classical clinical features of bladder pheochromocytoma like intermittent hypertension and post-micturition syncope were not observed in spite of careful observations.

The most important aid to the clinical diagnosis is the estimation of catecholamines in the blood or urine. Elevated values are observed in the vast majority of cases. Another test which has been found useful is the determination of Vanil Mandelic Acid (VMA) in the urine. In the present case there was a slight rise in the urinary catecholamines whereas value of VMA estimation was within normal limits.

The tumours present a pale brown, hæmorrhagic appearance at operation but very soon acquire a characteristic deep mahogany brown colour after a few hours fixation in formalin. On histologic examination the tumour shows a characteristic alveolar or lobular structure made up of large ovoid or polygonal cells. They show an abundant cytoplasm which exhibits a characteristic fine granularity. The vascularity of the tumour is striking with numerous thin-walled capillaries ramifying among the tumour cells.

Malignant behaviour has been observed in only 3 cases reported so far (Higgins and Tresidder, 1966). Histological appearance of the tumour is of no help in predicting the behaviour—the only evidence of malignancy being metastatic spread to regional lymph nodes and distant organs. Multicentric tumours are not uncommon (Albores-Saavedra *et al.*, 1969; Farley and Smith, 1959) and should not be mistaken for metastasis.

The surgical treatment of the tumour requires expert management owing to the wide fluctuations in the blood pressure observed during the manipulation and excision of the tumour. In the present case the blood pressure shot up to 220/115 mm. of Hg during manipulation followed by a precipitous fall to 100/60 mm. of Hg after the tumour was excised in spite of the fact that blood loss was negligible.

SUMMARY

A case of pheochromocytoma of the urinary bladder in a 65-year-old Hindu woman is reported. The only complaints were episodes of sudden painless hæmaturia. There was a complete absence of hypertension. The diagnosis was arrived at on biopsy examination, the laboratory investigations including the estimation of catecholamines and VMA being not of much help.

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PRUNE BELLY SYNDROME

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The prune belly syndrome consists of a triad of anomalies found almost exclusively in new-born males. These are absence or hypoplasia of the muscles of the abdominal wall, bilateral cryptorchism, and a urinary tract dilated proximal to the postatic urethra. Talipes, or other musculo-skeletal abnormalities, malrotation of the gut, and cardiac defects are sometimes associated. About 175 cases have been reported in the world literature.[2] Sixteen previously unreported cases have been seen in Pittsburg since 1953. The purpose of this paper is to review the syndrome and its management and to present these new cases.

Because of the weakened abdominal wall, the abdomen appears wrinkled and flabby and resembles a prune. This designation was first suggested in 1959 by McGovern and Marshall. As the boys grow older the wrinkles smooth out, the viscera hang low without support, and the body contour resembles a pear more than a prune.

The muscular weakness varies in degree and location, but is most common in the lower abdomen. Microscopic sections of the abdominal wall show either attenuated and atrophic muscle layers, or complete absence of the musculature leaving only skin, fascia, and peritoneum. Healing of abdominal wounds proceeds without incident, Attempts to tighten the wall surgically have been made (Williams and Burkholder, 1967; Stephenson, 1953), but are probably neither necessary nor successful. The weakness becomes less significant as the patients grow older. In infancy, the weak belly leads to flaring out of the lower chest and flattening of the diaphragm. The children are subject to respiratory complications because of their weakened cough mechanism. They are also prone to constipation.

In the rare cases where testes have been reported in the scrotum (Lattimer, 1958) the diagnosis is in question. The diagnosis is also doubtful in the few cases reported in females, but 4 of these may be justified. One of them is described below. Most of the females have some abdominal weakness, but their urinary tract has been normal. One of these cases is also reported below.

The most obvious urinary abnormality is in the bladder. It is usually tubular and often is attached to the umbilicus. The wall is thickened and hypertrophied, though not often trabeculated. Histologic examination reveals thickening and absence of elastic fibres. The bladder may be capped with a large urachal cyst, or the urachus may be patent. Bladder function cannot be correlated with the appearance of the organ as some empty, and others carry a high residual. Pressure and flow studies have been carried out (Nunn and Stephens, 1961; Williams and Burkholder, 1967). Anatomically obstructed bladders have high pressures, but in these, detrusor pressure was normal. These findings may not be universal, as the studies were carried out on children able to co-operate and who had survived the critical first 2 years during which half of those afflicted with this syndrome die. The trigone is frequently asymmetrical with the orifices high and lateral. The bladder neck is wide and tapering with dilation of the posterior urethra even in the absence of subvesical obstruction. Obstruction has been found in some patients. Bourne and Cerny (1967) feel that obstruction is an essential feature of the syndrome. They cited a case of a boy who had had numerous competent investigations, but the obstruction was not noted until he was 9 years old. Although others (Spence and Allen, 1964) feel that obstruction is not present, careful search must be made in each patient.

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[2] (Bourne, Cerny, 1967; Buke *et al.*, 1969; Eagle and Barrett, 1950; Lattimer, 1958; Mathieu *et al.*, 1953; McGovern and Marshall, 1959; Metrick and Brown, 1957; Nunn and Stephens, 1961; Silverman and Huang, 1950; Spence and Allen, 1964; Williams and Burkholder, 1967.)

The ureters are dilated, tortuous and flabby. They often are readily palpable, and with the distended bladder, fill the lower abdomen and flanks. Most show no function either by pressure studies or radiographically. Reflux is almost invariable. Ganglion cells are present, but the muscle is thinned, fibrous, hyalinised, and infiltrated with round cells. The kidneys may be absent, cystic, dysplastic in varying degrees, or hydronephrotic. Survival depends chiefly on the volume of functional renal parenchyma and its preservation.

The disease is not familial, and despite the fact that it occurs in males, it has not yet been reported in brothers. One boy with the syndrome had a normal twin brother (Howard, 1940). Chromosome studies have been normal in the few cases so studied (Williams and Burkholder, 1967).

Pathogenesis.—An early theory as to the cause of the triad was that the distention of the dilated urinary tracts caused muscular atrophy. However, in many cases with similar obstructive distention, the abdominal wall is normal. The converse was also proposed. Laxity of the body wall was supposed to cause passive distention of the urinary tract. But the absence of urinary anomalies in omphalocele or large hernias make this theory untenable. It has been proposed (Audren *et al.*, 1964) that estrogen may cause dilation of the bladder and ureters, and also cause failure of testicular descent. Something like this has been observed in mice (Gardner, 1935, 1936). The fact that the external genitalia of these boys are unquestionably male, and the fact that only 1 member of a set of twins was affected (Howard, 1940) contradict this theory.

Normally the intra-embryonic mesoderm differentiates into 3 portions during the third week. The paraxial or dorsomedial portion becomes the dermomyotome. The intermediate portion becomes nephrotome, and the lateral plates divide into the somatic and splanchnic mesoderm layers. By the sixth or seventh week the dermomyotome has migrated anteriorly, and ventral abdominal fusion has occurred. The metanephron is stimulated in the fourth to fifth weeks by the ureteral bud from the mesonephric (Wolffian) duct. Excretory tubules are formed as the collecting system branches. Excretion of fluid by the newly developing kidneys begins in the tenth week. Until this time, excretion takes place through the mesonephros (Arey, 1965).

In 1961 Nunn and Stephens postulated some insult to the embryo during the critical period from five to eight gestational weeks. Brierre, in 1963, suggested that the dilating abnormal ureters occupy the very plane through which the dermomyotome moves and in which the muscles develop. This blockade prevents normal muscular differentiation. This would correlate with the prevalence of the weakness in the lower abdomen, and also with the different degrees of muscular hypoplasia. A difficulty with this detailed theory is that ventral fusion of the abdominal wall and differentiation of the muscles is completed before secretion by the kidneys through the ureters begins. The embryology of the musculature of the trunk has not been studied to the extent of that of other organs, and it might be possible that some early insult might delay differentiation of these somites, and interfere with ureteral and renal development simultaneously. No tenable theory linking this syndrome to males has been suggested. The triad does not occur as a sex-lined recessive, as none of the males have ever been reported fertile, and no brothers have ever been affected.

Prognosis and Treatment.—The prognosis relates chiefly to the degree of kidney damage. Twenty per cent die within the first 2 weeks of life, and 50 per cent in the first 2 years. An aggressive approach in the new-born may lead to tiding marginal cases over long enough until they are ready for definitive therapy. After diagnostic radiographic and biochemical studies, early decompression is essential. Marshall suggests bilateral nephrostomies (McGovern and Marshall, 1959; Waldbaum and Marshall, 1970). We favour cutaneous loop ureterostomies in order to avoid the many problems of the foreign body. Subsequent operations are carried out if the renal parenchyma proves adequate enough to support life. These procedures would include tailoring and shortening of the ureters, pyeloplasties, revision of the bladder neck, and neoureterocystostomy. Urinary diversion by ileal conduit is necessary in those cases where the more conservative measures fail to provide adequate drainage and freedom from infection. Two ileal loops have been reported (Buke *et al.*, 1969) and a third was done here in 1969. It is reported below.

Orchiopexy is rarely reported. The literature records only 5 such operations (Williams and Burkholder, 1967; Waldbaum, 1970). In 4 of these, the procedure was done in 2 stages because of the distance of the testes from the scrotum. At the same time that the ileal loop was done here in 1969, orchiopexy was performed. Both spermatic vessels were divided because they were too short. These testes have survived without atrophy on the blood supplied through the artery of the vas deferens. Two other patients in this series have also had orchiopexy, and 3 of these spermatic vessels were divided. It is not correct to say that this condition causes sterility (Williams and Burkholder, 1967), as only 1 of these cases has been followed into adulthood. Eventual studies on these 8 patients regarding potency and fertility will be desirable.

CASE REPORTS

Of the 16 cases in this series, 9 are alive, 6 have died, and 1, lost to follow-up, is presumed dead. Of the 6 that died, the oldest, (D. L., CHP No. T-10514) was 13 months of age. Though the ethnic origin of the reported cases is usually not specified, this is the only one to my knowledge who was negro. He died of pneumonia in 1956. The other 5 died in kidney failure before they were 2 months old. The most recent death was that of a boy, (J. M., CHP No. 16-66-36) weighing 2·6 kg. (5 lb. 13 oz.), the product of an uncomplicated 37-week pregnancy. He was cyanotic at birth and was admitted to Children's Hospital 8 hours later. The physical findings were typical. The bladder and ureters were palpable; urinary output was negligible. The urine culture grew *Pseudomonas*. Cystography showed a cone-shaped bladder and bilateral ureteral reflux into patulous ureters. Kidney details were not discernible. When he was 7 days old he had bilateral ureterostomies. Neither kidney was large enough to palpate at surgery. Urinary output did-not increase appreciably post-operatively. He died at the age of 2 months with a BUN of 210 mg. per cent and a falling sodium and potassium. Autopsy permission was refused. We assumed that both kidneys were dysplastic.

The oldest survivor in this group of patients (R. H., CHP No. R-1947) is 18 years old. At the age of 2 months he had revision of the bladder neck and suprapubic cystostomy. The tube was removed when he was 2 years old. Since then he has voided well with only rare bouts of infection. The right kidney has atrophied and the left shows compensatory hypertrophy. He was last seen 3 years ago at which time excretory urography showed a satisfactory left kidney.

The next oldest (S. C., CHP No. W-10-091) was born in 1958. The bladder was duplex with ectopic ureteral orifices. He has had in his childhood revision of the bladder neck, bilateral shortening of the ureters, right ureterolithotomy, several left ureterolithotomies, and left nephro-ureterectomy. His last pyelogram was 3 years ago, and showed good function and no stones. He is asymptomatic. The parents say that " he has had enough operations " and are unwilling to consider orchiopexy.

One of the 2 ten-year-olds (G. D., CHP No. 3-03-74) had bilateral shortening of the ureters and suprabuic drainage in infancy. He is seen regularly, and has a normal BUN. Attempts to remove the suprapubic tube have been unsuccessful and as he tolerates the tube well other diversion is not planned. He recently had bilateral orchiopexy; one of the spermatic vessels needed to be divided to place the testis in the scrotum.

The other ten-year-old (J. T., CHP No. 3-49-17) had repeated problems with urinary infections. Diversion was suggested at age 4, but was not accepted until 5 years later. At that time, 1969, he was in diapers because of dribbling overflow incontinence, and had had repeated admissions for the control of pyelonephritis. Four months after the ileal loop urinary diversion the left ureter was further shortened, and since then he has been free of infection. He is able to attend school for the first time. He had the simultaneous orchiopexy described above.

R. W. (CHP No. 19-04-30) was first seen here at the age of nine for orchiopexy. He had had only two known bouts of urinary infection at the age of 3 months and 5 years. When first seen in the clinic, urinalysis and culture were normal, but on admission, 3 months later, more than a million colonies of *E. Coli* were found in the urine. He was asymptomatic on both occasions. The BUN was 14 mg. per cent; the excretory urogram showed bilateral caliectasis, pyelectasis, and ureterectasis. The voiding cystogram showed a cone-shaped bladder but no reflux. This probably saved his kidneys from destruction during the many infections which he must have had. Bilateral orchiopexy with division of the spermatic arteries was performed, and 6 months later the testes were unchanged in size.

A seven-year-old (R. B., CHP No. 8-35-44) has a normal twin brother. The excretory urogram showed right caliectasis and left renal ectopy. He has been managed without urologic surgery, but has had several orthopædic procedures for anomalies of the extremities.

The boy lost to follow-up (R. D. CHP No. 8-93-86) was last seen in 1966 at the age of 16 months. Bilateral nephrostomies had been performed, but one of the kidneys was not functioning. He is presumed dead.

The seventh survivor (D. B., CHP No. 4-18-69) is especially interesting in that she is a female. Born in 1960, she had the typical prune belly syndrome. The extremeties were normal, and chromosome studies were female. She had moderate ureterectasis and tortuosity. The kidneys were not dilated. The bladder was slightly hypertrophied, but the orifices were normal. Two years ago, in another city, she had right lower lobectomy for bronchopulmonary sequestration. This anomaly has not been seen previously in prune bellies. Her parents deny her having any recent urinary difficulties.

Eight of the 175 reported cases have been female. Five of these had no urinary abnormalities, so had only one of the criteria of this syndrome. One girl reported by Buke (1969), one by Mathieu *et al.* (1953), one by Marshall (1970), and these are the only ones that had urinary dilation as well as weakness of the abdominal wall.

The last 2 survivors are still infants. One is a girl (B. G., CHP No. 17-29-51) 3 months old who has defective abdominal muscles, but whose urograms and urine studies are normal. She has needed 2 orthopædic operations. The other is a boy (A. A., CHP No. 17-30-95) 2 months old whose X-ray shows dilation of the calyces, pelves, and ureters. The 30-hour post-injection film showed retained contrast in the right kidney. On his fourth day of life *Klebsiella* was found in the urine. He needed suprapubic compression to empty the bladder. On his sixth day he had bilateral loop ureterostomies. Biopsy of the right kidney was normal except for a microscopic cyst.

DISCUSSION

No single programme of optimum management for the child with the prune belly syndrome can be presented, as the degree of renal damage varies so much from child to child. In the child with severe renal damage, neonatal ureterostomies may be essential to survival. They then become a challenge to the pædiatrician because of their susceptibility to respiratory infections as well as electrolytic difficulties or the more mundane constipation. They must be followed closely to preserve the renal reserve which is present and antimicrobial therapy is indicated to keep them infection free. When older, urologic surgery such as bladder neck revision, cystoplasty, neoureterocystomy, tailoring of the ureters, or urinary diversion are carried out as indicated in each individual. Orchiopexy should be included in the overall plan. Many of the children will also need orthopædic care because of anomalies of the extremities.

SUMMARY

The Prune Belly Syndrome is a congenitally occurring group of anomalies found almost exclusively in new-born males. The three principle features are absent or hypoplastic musculature of the abdominal wall, bilateral cryptorchism, and dilation of the urinary tract. Early drainage of the kidneys by bilateral cutaneous loop ureterostomies may be necessary to preserve borderline renal function until the child matures enough to have surgery to provide adequate drainage and freedom from infection. The cause of the syndrome is probably some undetermined insult to the embryo between its fifth and eight gestational week. One hundred and seventy five cases have been previously reported; 16 cases seen in Pittsburg since 1953 are reviewed with the principles of management.

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EPIDERMOID CYST OF THE TESTIS

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BENIGN tumours of the testis are rare. Epidermoid cyst accounts for about 1 per cent of the testicular tumours in the American Testicular Tumour Registry (Price, Jr., 1969). Of 97 cases of epidermoid cyst of the testis recorded in the literature (Price, Jr., 1969; Gilbaugh, Jr. *et al.*, 1967; Ewen, 1969) only 2 have previously been reported from Britain (Ewen, 1969; Halley, 1961).

CASE REPORT

A 45-year-old white male sought surgical advice with a 6 months' history of gradual painless enlargement of the left testis. A provisional diagnosis of testicular tumour was made and orchidectomy performed.

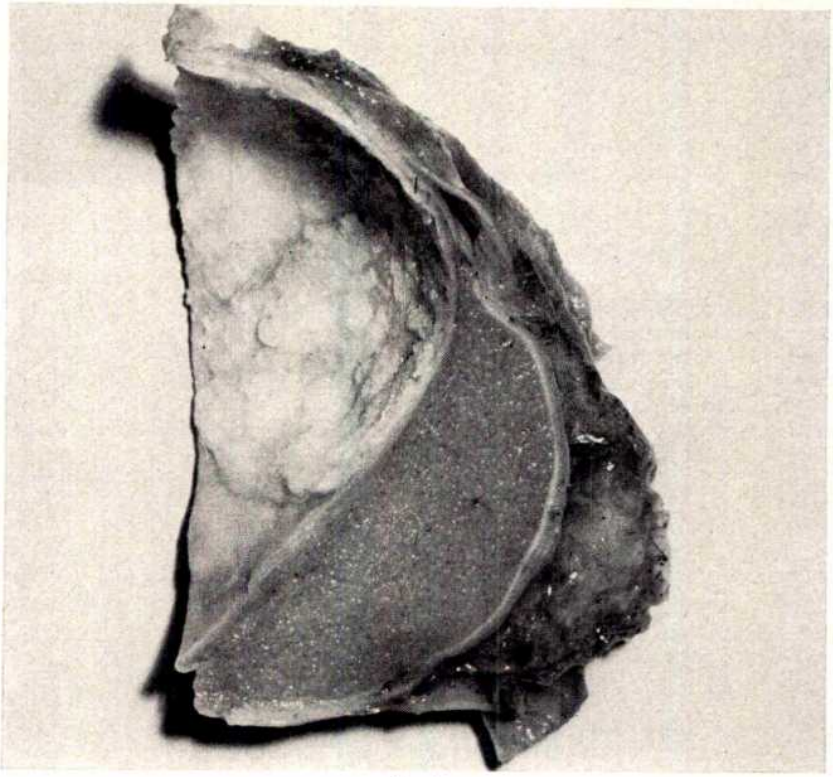

FIG. 1

Bisected testis with epidermoid cyst. Most of the contents of the cyst have been removed exposing the pearly white inner lining.

Gross Pathology.—The specimen consisted of an enlarged, firm, ovoid testis, 7·5 × 5·5 × 4·5 cm. with 8·5 cm. of attached spermatic cord. Within the lower pole of the testis there was a unilocular, well-circumscribed ovoid cyst surrounded by 2-10 mm. of testicular parenchyma. The cyst contained white greasy material similar to sebum, had an irregular, pearly white inner lining and a white capsule approximately 2 mm. thick. The epididymis appeared normal (Fig. 1).

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Histopathology.—The cyst contained laminated keratin and had a wall consisting of fibrous tissue supporting an almost complete lining of well-differentiated, keratinising, stratified, squamous epithelium varying from 2-10 cells thick (Fig. 2). In most areas well-defined basal cell, squamous cell and granular cell layers were easily identified. Mitotic figures, pleomorphic nuclei and premature keratinisation were not present. Focal aggregates of lymphocytes were present exterior to the capsule but inflammatory reaction of foreign-body type, calcification or ossification were not present. No skin appendages or teratomatous elements were present in the cyst wall or testicular parenchyma. The seminiferous tubules were essentially normal showing active spermatogenesis but some tubular compression and atrophy were noted immediately subjacent to the fibrous capsule. No squamous metaplasia was present in the seminiferous tubules, rete testis or epididymis. Interstitial cells were normal in number but there was some interstitial œdema.

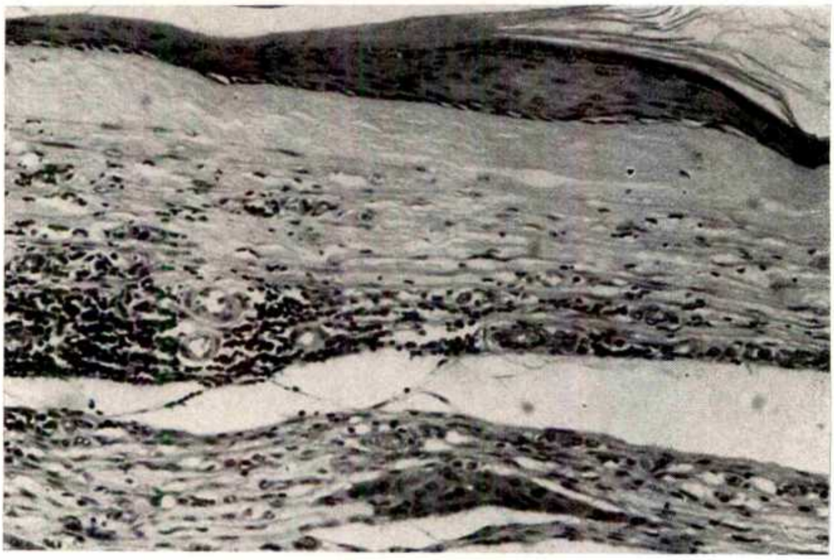

FIG. 2

Wall of epidermoid cyst with characteristic keratinising stratified squamous epithelium and lack of adnexal skin structures.

DISCUSSION

The majority of testicular tumours are malignant and it has become almost universal surgical practice to remove any testicular mass and subject it to histopathological examination. Epidermoid cyst of the testis is a rare lesion. Until 1969 only 31 cases had been recorded in the world literature (Gilbaugh, Jr. *et al.*, 1967; Ewen, 1969). However, Price (1969) reviewed the records and microscopic slides of 5,845 testicular tumours—an unprecedented volume of material—and found 69 cases which qualified under his criteria for the designation of epidermoid cyst of the testis. Three of the 69 cases had been previously reported.

It is important to make the distinction between an uncomplicated epidermoid cyst and a teratoma as the latter is usually regarded as having malignant potential. The histological criteria for epidermoid cyst listed by Price (1969) are recommended, *viz.*, (1) a cyst wholly within the testicular parenchyma, (2) a cyst containing keratin, (3) the cyst wall consisting of a fibrous capsule and lined by a well-differentiated, keratinising, stratified, squamous epithelium, and (4) no skin appendages or teratomatous elements in the cyst wall or testicular parenchyma. A certain laxity of terminology has existed in former times; such terms as epidermal cyst, epidermoid cyst, squamous cyst, dermoid cyst, benign teratoma and differentiated teratoma being employed at random. An epidermoid cyst is one lined by stratified squamous epithelium and filled with keratin but without skin appendages in its wall. A teratoma is a tumour composed of derivatives of the 3 primitive germ layers in varying combinations, and is designated benign (adult) or malignant according to the degree of maturation of any of its histological elements (Weitzner, 1964).

The histogenesis of epidermoid cyst of the testis is unknown. The major consensus of opinion is that it is a monodermal development of a teratoma. If this is correct then it immediately raises the question; does epidermoid cyst of the testis have the potential malignancy of a teratoma? Long-term follow-up of patients who have had orchidectomy for epidermoid cyst of the testis support the benign nature of this lesion (Price, Jr., 1969; Gilbaugh, Jr. *et al.*, 1967). It would be presumptuous to suggest that if left alone this lesion would eventually develop into a classical teratoma. Olsen and Calderin (1955), Halley (1961), and Ewen (1969) suggest an origin as a result of squamous metaplasia in seminiferous tubules or rete testis.

Although the histogenesis of epidermoid cyst is apparently distinct from that of a benign teratoma, it has been alleged that an epidermoid cyst may co-exist with a teratoma or other testicular neoplasm (Cook, Jr. and Kimbrough, 1954; Weitzner, 1964). Consequently, biopsy or simple enucleation of such a cyst does not exclude the presence of such a co-existing neoplasm elsewhere in the affected testis. An additional diagnostic point to those listed by Price is, therefore, suggested, *i.e.*, all of the cyst and testis be submitted for histopathological examination.

Simple uncomplicated epidermoid cyst of the testis appears to be a benign lesion and recurrence or metastasis have not been reported. The earliest recorded case was that of Dockerty and Priestley (1942) and the patient was well 24 years later (Gilbaugh, Jr. *et al.*, 1967). In the series examined by Price, patients were well up to 15 years after operation. Orchidectomy, without retroperitoneal lymph node dissection or post-operative radiotherapy is therefore the treatment of choice.

SUMMARY

A case of epidermoid cyst of the testis is described. This lesion appears to be completely benign and the prognosis after orchidectomy is good.

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EPIDERMOID CYST OF THE TESTICLE

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The initial treatment of testicular tumour is universally accepted as being orchiectomy. The incidence of benign tumours is so low that the risk of unnecessary removal of the testis is accepted. A recent case of epidermoid cyst of the testicle leads to a review of the literature on benign testicular tumours and consideration of their diagnosis, origin, and treatment.

Review of the Literature.—Twenty-three cases of epidermoid testicular cysts have been reported in the world literature.[2] The age range of these patients is from 14 to 59 years with a median of 28 years. The size of the tumours ranged from 0·4 to 5·0 cm. in diameter with a median of 1·6 cm. The clinical findings were indistinguishable from those of malignant tumours. Two-thirds of the men presented with painless masses, and almost half of these had tumours discovered incidentally on routine physician examinations.

In 1954, Cook and Kimbrough reported that they distinguished benign from malignant lesions by palpation and inspection after incising the albuginea. If benign, they performed local excision of the lesion. This is unsatisfactory as many microscopic sections are required to exclude the diagnosis of teratoma or teratocarcinoma. Even the former is known to metastasise.

Pathogenesis.—The origin of epidermoid cyst is not clear. Halley (1961) postulated that these cysts represent keratinising cysts of the rete testis. But squamous metaplasia, though occurring in the vas and epididymis has not been reported in the rete or in the seminiferous tubules. Also, some of these cysts do not occur near the rete. Weitzner (1964*b*) suggested that these represented epidermal inclusion cysts, but offered no proof. He also proposed, more plausibly, that one of the germ layers of a teratoma develops unilaterally or monophyletically. The so-called stem cell is totipotential, and teratoid lesions contain 1 or more of the 3 germ layers developed to varying degrees. In the epidermoid cyst only the epidermal portion of the ectoderm develops. Cook and Kimbrough's teratoma had only a tiny adjacent cyst containing intestinal and respiratory epithelium. Most of the lesion was the epidermoid cyst. The uncertainty of the underlying nature of these allegedly benign cysts is emphasised by one of Weitzner's cases who died of disseminated choriocarcinoma. The only lesion found in the testes was an epidermoid cyst. Despite careful search at post-mortem no identifiable primary was found. Follow-up on the cases in the literature is inadequate. The longest was for 7 years (Weitzner, 1964*b*). Most were reported at the time of surgery.

CASE REPORT

H. L. (WPH No. 32-74-13) was admitted to The Western Pennsylvania Hospital on 19th November 1970. He was 32 years old, and had had a mass found in the left testis on routine pre-employment physical examination. He believed that the left testis may always have been slightly larger than the right. He thought that the mass may have been present for 5 to 6 months, and also reported a mild ache in the left testis especially following coitus. With the exception of the left testis, physical examination was completely normal. A firm, non-tender mass, 1 cm. in

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[2] (Dockerty and Priestly, 1942; Gage and Brodie, 1950; Mooslin and Schulte, 1951; Jensen, 1952; Cook and Kimbrough, 1954; Nagel and Polley, 1955; Olsen and Calderin, 1955; Delinotte and Gouzon, 1956; Mathe, 1957; Nowlin *et al.*, 1959; Samuel and Tweedale, 1961; Halley, 1961; Wohumani, 1962; Weitzner, 1964*a*; Weitzner, 1964*b*.)

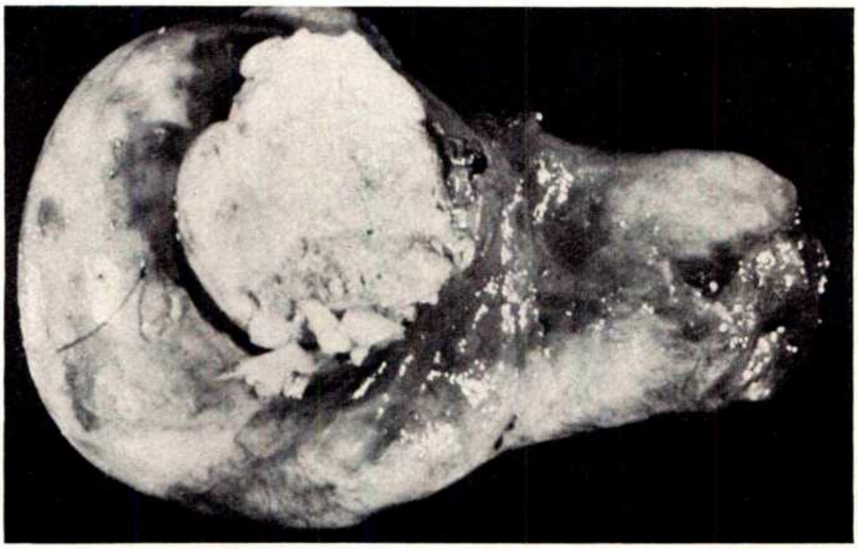

FIG. 1.—Gross specimen after unroofing of cyst, showing keratin-filled cyst at upper pole left testis.

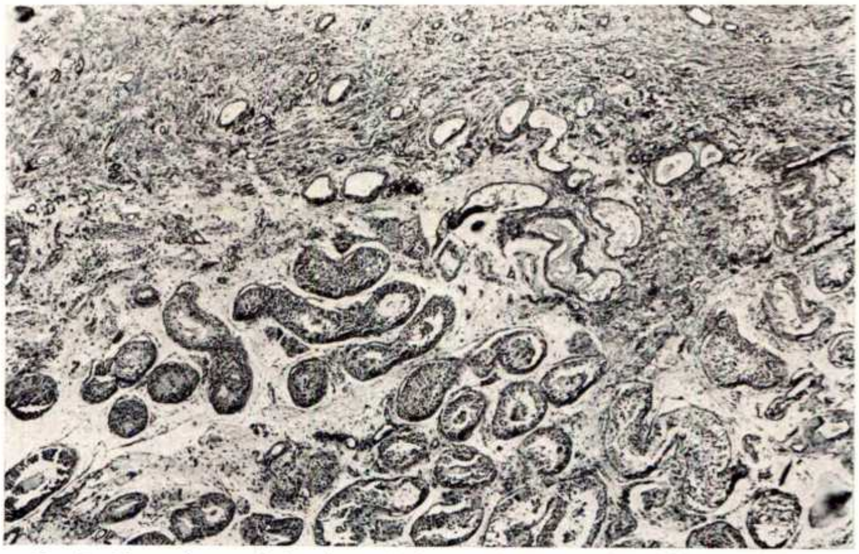

FIG. 2.—Photomicrograph showing wall of cyst and compressed seminiferous tubules. (H. & E. Reduced from × 36).

diameter was situated posteriorly and superiorly on the left testis. Lymphadenopathy, abdominal masses, and gynæcomastia were not present. Laboratory studies including complete blood count, urinalysis, 12-channel screen[1], urinary chorionic gonadotrophins, and radiographic studies of the chest and urinary tract were normal. Through an inguinal incision the cord was isolated and occluded with a tourniquet. The testis was delivered and a firm white nodule at the upper pole resembled a seminoma. When a segment was removed for frozen section, thick grumous material exuded. The albuginea was further incised, and a round cyst 3 cm. in diameter came away without attachment either to the testis or albuginea. Despite the histologic report of no malignancy, the testis and

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[1] Blood urea nitrogen, glucose, bilirubin, cholesterol, calcium, inorganic phosphorus, uric acid, alkaline phosphatase, protein, albumin, lactic acid dehydrogenase (LDH), and serum glutamine oxalic transaminase (SGOT).

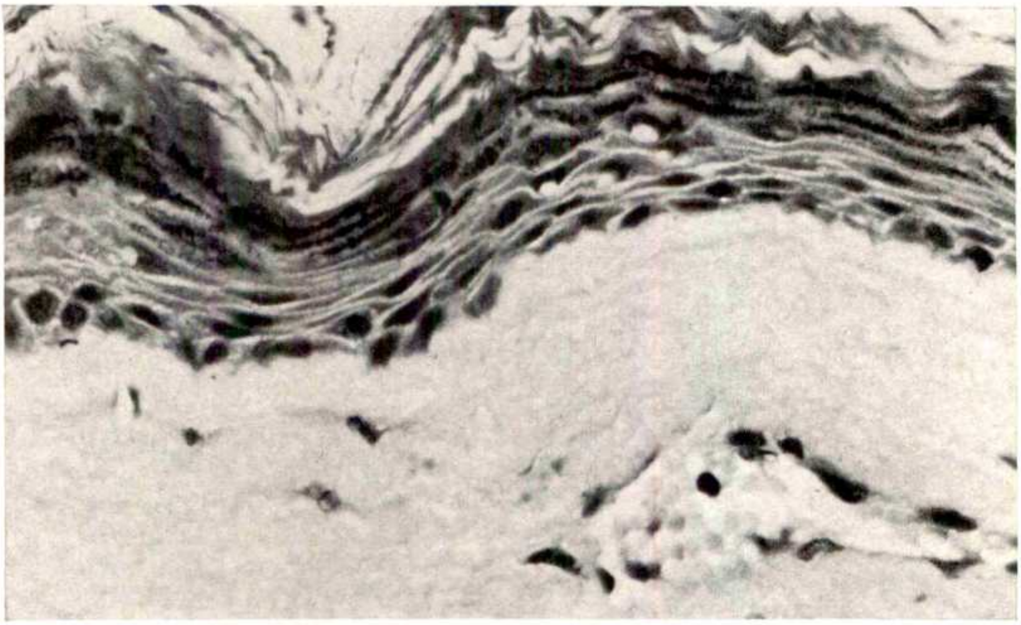

FIG. 3.—Photomicrograph of wall of cyst showing desquamating epidermal cells. (H. & E. Reduced from × 240).

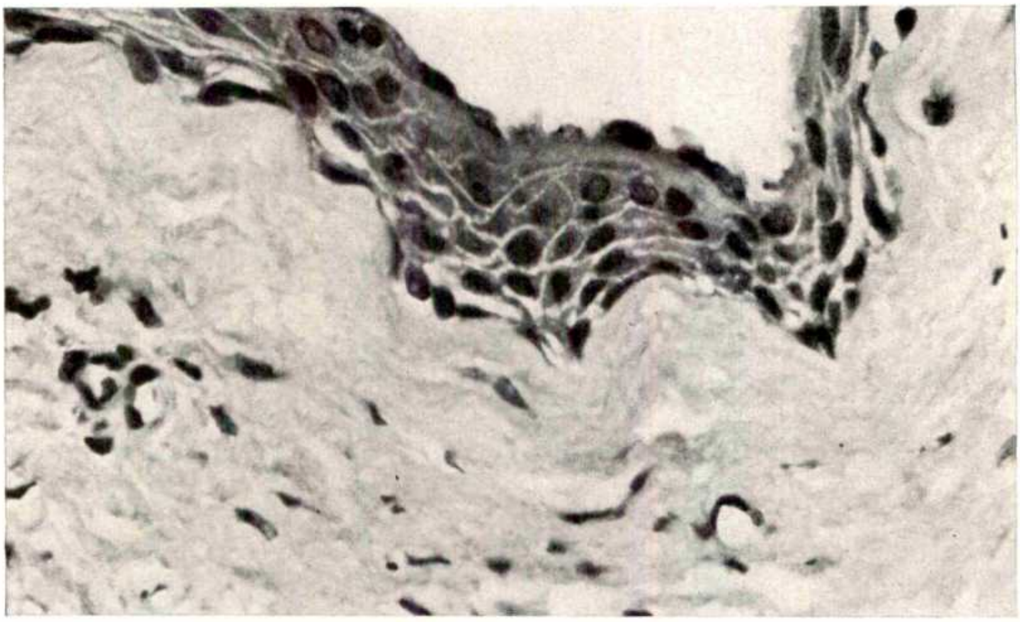

FIG. 4.—Photomicrography of wall of cyst showing intact basement membrane and mature squamous epithelial cells (H. & E. Reduced from × 240).

cord were removed. The final diagnosis stated that the lining of the cyst was squamous epithelium with a fibrous wall. The surrounding testis showed compressed normal seminiferous tubules. The cyst contained keratin (Figs. 1 to 4). He recovered from surgery without complication and continues to do well. No further treatment is planned.

DISCUSSION

Collins and Pugh (1964) reviewed 995 cases reported to the Testicular Tumour Panel and Registry in Great Britain from 1958 to 1963. Of these, 13 were classified as teratomas, differentiated. Six of these were adults; 2 of these were dead with metastases, and a third with radiation nephritis. Two of the 6 (presumed alive) had tumours " almost entirely squamous ". They say that " no tumour of the testis is characterised as benign since this property cannot be ascribed with any security even to the most differentiated teratoma ". Herbut (1952) claims that 2 to 4 per cent of all testicular tumours are benign. Mostofi was quoted as believing that the incidence was higher (Olsen and Calderin, 1955). In view of the probable origin of these epidermoid cysts from the totipotential stem cell of teratomas, it seems risky to treat them as though they were benign. Complete orchiectomy should be the operation of choice. But since, like childhood teratomas, they appear to behave benignly, radiation and/or node dissection following orchiectomy can be avoided. The question at the time of surgery for testicular mass should not be: is this benign or malignant, but is this lesion neoplastic or inflammatory? The pathologist can answer this question, and only if the ætiology is inflammatory may the testis be left in place.

SUMMARY

The twenty-fourth case of epidermoid cyst of the testis is described with a review of the literature and of theories of the origin of this tumour. It is concluded that all neoplasms should be treated by complete orchiectomy through a groin incision. Although epidermoid cysts appear benign, the malignant potential of already disturbed germ cells is too great to leave the testis behind.

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THE RELATIONSHIP BETWEEN BACTERIAL CULTURES OF THE VAGINAL INTROITUS AND URINARY INFECTION

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Most urine infections in women appear to develop in an ascending manner. The probability of an infection developing may therefore depend on the frequency of bacterial inoculation into the bladder and urethra, on the size of the inocula, on factors influencing the rate of bacterial multiplication and death in urine and tissue, and on the hydrokinetic clearance of bacteria.

The urethral flora is rich, and may include potentially pathogenic Gram-negative bacteria (Cox, Lacy and Hinman, 1968). It is influenced qualitatively by the flora of the rectum (Spencer, Mulcahy, Shooter, O'Grady, Bettleheim and Taylor, 1968; Grüneberg, 1969), the vagina (Cox *et al.*, 1968) and the vestibule (Grüneberg, 1969). Therefore it would seem possible that profuse colonisation of the vestibule with *Esch. coli* would predispose to urinary infection, and that factors influencing the degree of such colonisation would secondarily affect the incidence of urinary infection. Evidence in favour of the first hypothesis was presented by Stamey (1968), and claims have been made that perineal hygiene is important in the genesis of urine infection (Moore and Hira, 1965; Gibbon, 1970). However, a pilot study conducted by us did not confirm this hypothesis. We have, therefore, investigated the significance of the vaginal introital flora in a prospective study and have tried to assess the relevance of certain other factors which might influence the introital flora or the occurrence of urine infection.

Patients and Methods.—191 patients with symptoms suggestive of recurrent urine infection were investigated in a special clinic. Race, age, marital and menopausal status, contraceptive habit and details of pregnancies were recorded routinely. In most patients information concerning coital frequency, menstrual protection and perineal toilet hygiene was obtained. Intravenous pyelograms were obtained in all, micturating cystograms in most. Patients were told to return to the clinic at once should symptoms recur, and were reviewed monthly for 6 months after an infection, then less often if they remained free from infection. They were questioned at each visit about antibacterial therapy received from other sources.

Over a 15-month period introital swabs, together with mid-stream (and occasional suprapubic aspirate) urine specimens, were taken at each visit from the 191 women studied; they were not taken during heavy menstruation. The introital swabs were collected first. As a standard procedure, a moist sterile cotton wool swab was passed once round the internal margin of the uncleaned vaginal introitus, inserted into a bijou bottle containing 5 ml. of sterile 0·85 per cent saline and kept at 4°C. Within 5 hours the swab was removed after pressing it lightly against the bottle neck, and 0·1 ml. of the resulting mixed suspension was plated on blood and MacConkey agar, for aerobic incubation. Preliminary experiments showed no difference between swabs taken in parallel and suspended in saline and tryptone water. This acted as a control on the use of saline as a transport medium and also provided a check on reproducibility. After collection of an introital swab the perineum was cleaned in an antero-posterior direction with gauze soaked in sterile saline, and a mid-stream urine (M.S.U.) specimen was obtained and refrigerated at 4°C. Within a few hours it was cultured quantitatively using a surface viable counting technique (Miles and Misra, 1938). Bacteria exceeding 10,000 per ml. in M.S.U. specimens, any bacteria cultured from suprapubic aspirates, and lactose fermenters cultured from introital swabs were identified according to Cowan and Steel (1965).

The relationship between cultures made from the swabs and from the urine passed immediately afterwards was studied on 808 occasions in the 191 patients. The bacteriology in all those who had 3 or more swabs collected, providing a total of 476 swab-M.S.U. pairs in all, was studied in more detail.

The prognostic significance of introital swabs with regard to the subsequent development of urinary infection was examined in 83 of the original 191 patients. The criteria for selection of these 83 patients were a follow-up of at least 3 months and 3 visits, and the absence of antibacterial treatment (from whatever source), during follow-up, in those remaining free of infection. Such therapy might have interfered with the development of a urine infection. The other 108 patients did not meet at least one of these requirements and the prognostic significance of their swabs was not considered.

TABLE I

The Development of *Esch. coli* Urine Infection during follow-up, in relation to the results of the Initial Introital Swab Cultures

Growth of *Esch. coli* from First Swab	Number (and designated group) of Patients	Number of Patients Infected* during follow-up	Per cent Infected
No growth	47 (A)	19	40·4
1-49 per ml.	14 (B)	10	66·6
50-2,000 per ml.	14 (C)	9	
Over 2,000 per ml.	8 (D)	5	

No growth (Group A) *vs.* Any growth (Groups B-D):
$\chi^2 = 4{\cdot}6204$, 0·05 > P > 0·025, $2\alpha = 0{\cdot}05$.

* Any of the following, separately or in combination:
2 consecutive M.S.U. specimens culturing 100,000 or more *Esch. coli* per ml.
1 M.S.U. specimen culturing 100,000 or more *Esch. coli* per ml., with an uncentrifuged urinary leucocyte concentration exceeding 10 per cu. mm.
1 M.S.U. specimen culturing 100,000 or more *Esch. coli* per ml., collected when there was pain during micturition.
1 suprapubic aspirate culturing any number of *Esch. coli*.

The 83 patients referred to above were analysed according to the results of their initial introital swab cultures (taken when the patients were not receiving antibacterial agents, and their urine was not infected) and whether or not they became infected during follow-up. A patient's follow-up was taken from the time of collection of her first swab until her last visit before the end of the study. Patients were classified on the basis of their initial introital swab counts into Groups A-D as defined in Table I.

The results of the first two consecutively obtained swabs were similarly used to further classify the patients according to whether or not *Esch. coli* were cultured from both swabs. Patients from whose swabs *Esch. coli* were grown on only one of the two occasions were excluded from this analysis.

The criteria for definition of urine infection are shown in Table I.

Fisher exact probability, Chi square, Student t, and Mann-Whitney U tests were performed where appropriate (Siegel, 1956).

Results.—*Comparison of Cultures made from Introital Swab and Mid-stream Urine Specimens.*—Figure 1 shows the results of the 808 paired introital swab and urine cultures. In patients not

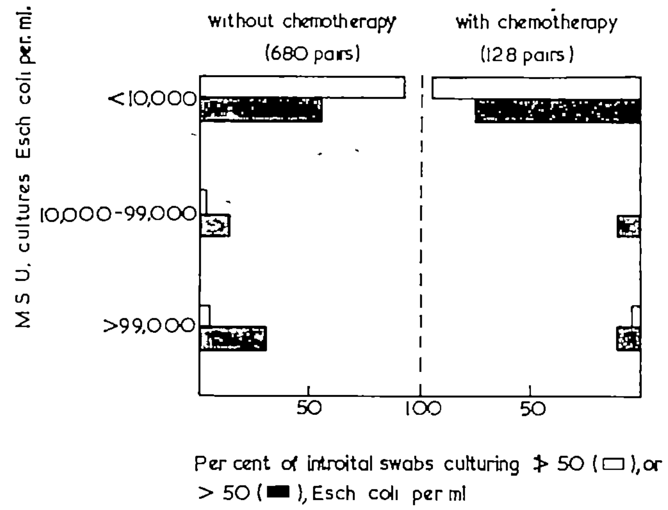

FIG. 1
Relationship between paired introital swab and mid-stream urine cultures.

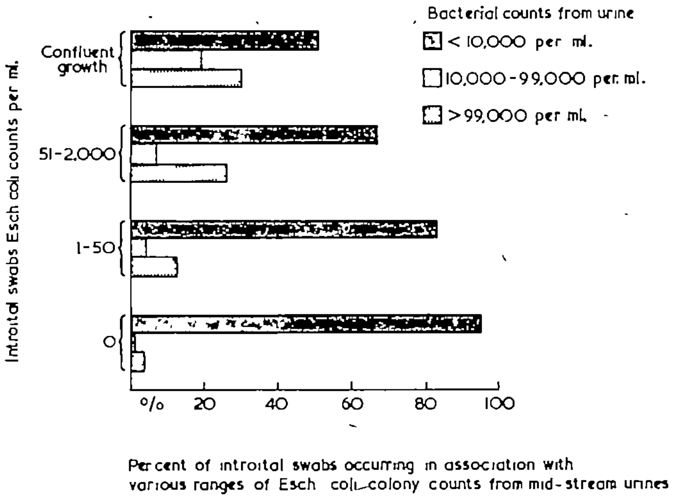

FIG. 2
Detailed relationship between paired introital swab and mid-stream urine cultures.

receiving antibacterial therapy 4·2 per cent of swabs from which 50 or less *Esch. coli* per ml. were cultured (" low count " swabs), and 29·6 per cent of those from which more than 50 *Esch. coli* per ml. were obtained (" high count " swabs), were associated with a urinary count of 100,000 or more *Esch. coli* per ml. The difference was highly significant ($X^2 = 134{\cdot}5248$, $P < 0{\cdot}005$). When specimens taken from patients receiving antibacterial treatment were considered, 3·6 per cent of the " low count " and 12·5 per cent of the " high count " swab cultures were associated with a urine culture of 100,000 or more *Esch. coli* per ml. This difference with and without chemotherapy was not significant.

The more detailed results of the 476 paired swab and urine cultures referred to earlier, collected when the patients were not receiving antibacterial therapy, are illustrated in Figure 2. The urinary *Esch. coli* count increased significantly with the introital swab count ($P < 0{\cdot}0005$).

Development of Urinary Infection in Relation to the Introital Swab Cultures.—The relationship between cultures made from the first introital swabs and the subsequent development of *Esch. coli* urine infections is shown in Table I. 40·4 per cent of patients from whose first swab no *Esch. coli* were cultured (Group A) became infected, compared with 66·6 per cent of those from whom *Esch. coli* were obtained (Groups B-D). This difference was significant. Surprisingly, patients from whose swabs large numbers of *Esch. coli* were cultured appeared no more likely to develop urine infections than those from whose swabs few were grown (although the numbers in each group were too small to be certain of this).

TABLE II

The Development of *Esch. coli* Urine Infection During follow-up in relation to the results of the First 2 Introital Swab Cultures

Growth of *Esch. coli* in each of the First 2 Swabs	Number of Patients	Number of Patients Infected* during follow-up
No growth	26	6
Some growth	8	6

" No growth " *vs.* " Some growth ": $P = 0{\cdot}0127$, $2\alpha = 0{\cdot}05$.
* See legend to Table I.

The results of cultures made from the first 2 introital swabs are shown in relation to the subsequent development of infection in Table II. Once again there was a significant difference between patients from whose introitus no *Esch. coli* were cultured, and those from whom some were obtained. However, the prognostic value of the two swabs, considered together, was not significantly better than that of the initial swab, considered by itself.

Follow-up after the first introital swab exceeded 3 months and 3 visits in all patients, but was otherwise variable. However, the length of follow-up of patients from whose first swab no *Esch. coli* could be cultured (63·6 ± S.E. 3·3 weeks) was similar to that of patients from whose first swab some were cultured (64·7 ± S.E. 4·0 weeks; $t = 0{\cdot}2062$, $P > 0{\cdot}05$). Therefore variations in duration of follow-up could not be held responsible for the above findings.

Rapidity of Development of Infection (Table II).— The mean time taken to develop infection (taking into account only those who developed an infection) was greater in patients from whose introitus no *Esch. coli* could be cultured than in those from whom some were obtained. However the ranges involved were large and the groups did not differ significantly in the distribution of these intervals.

Factors examined in relation to the Degree of Bacterial Colonisation of the Introitus, and to the Development of Urinary Infection during Follow-up.—Certain factors were analysed to see if they influenced the degree of bacterial colonisation of the vaginal introitus at the first examination. These factors were race, age, catamenia, marital status, gravidity, coital frequency, use and type of contraceptives, menstrual protection, perineal hygiene, and radiological abnormalities of the urinary tract.

All except 2 of the 83 women were Caucasian, and only 5 were single. 44 out of 47 Group A patients (94 per cent) and 30 out of 36 Group (B-D) patients (83 per cent) were pre-menopausal (an insignificant difference). The mean age of Group A and Group (B-D) patients was 31·4 and 34·2 years respectively, and the groups did not differ in their age distribution ($U = 722·0$, $Z = 1·15$, $P > 0·05$). Details of coital frequency were known for 76 patients; there was no significant difference between patients in the two groups in this regard. Neither did the groups differ in the choice (mechanical or oral) of contraceptives. Information concerning menstrual protection was obtained from 56 of the pre-menopausal women, and concerning perineal hygiene from a similar number; the patient groups did not differ in the distribution of those who were not asked, or preferred not to answer, questions concerning these factors. There was no significant difference between the groups regarding the use of external or internal menstrual protection, the regular use of toilet tissue after micturition or the directional use of perineal cleansing after micturition or defæcation.

TABLE III

Patients who Developed *Esch. coli* Urine Infection during follow-up: Time from collection of the First Swab to finding of Infection, in relation to the results of Culture of the Swab

Growth of *Esch. coli* from the First Swab	Mean Time (and range) to Infection, in weeks
No growth	25·7 (2-86)
Some growth	16·2 (1-48)

$U = 192·0$, $Z = 0·9$, $P > 0·05$, $2\alpha = 0·05$.

Intravenous pyelograms of satisfactory quality were obtained in 77 of the 83 patients. Six out of 44 Group A and 5 out of 33 Group (B-D) patients had classical radiologically defined chronic pyelonephritis, and the prevalence of all major radiological abnormalities was almost identical in the 2 groups. Micturating cystograms were obtained in 57 patients; vesico-ureteric reflux was observed in only 3.

In addition the same factors were examined to see if they influenced the development of *Esch. coli* urine infections in our patients, independent of any effect on the introital flora. Their prevalence in patients who became infected during follow-up was compared with that in patients who did not become infected. Infected and non-infected patients differed only in so far as age and catemenia were concerned. The mean age of patients who become infected during follow-up was 35·8 years (range 20-65), and that of patients who did not do so was 29·2 years (range 13-57). This difference was significant ($U = 613·0$, $Z = 2·3$, $P = 0·01$). Eight out of 43 infected patients (19 per cent), and 1 out of 40 non-infected ones (3 per cent), were post-menopausal. This difference was also significant ($X^2 = 4·0184$, $0·05 > P > 0·025$).

DISCUSSION

We have demonstrated a positive correlation between the degree of colonisation of the vaginal introitus with *Esch. coli* and the bacterial counts of mid-stream urine specimens collected a few minutes later. Several factors may have contributed to this finding. A high concentration of bacteria in the vestibule might have produced raised bacterial counts in the urine through contamination; introital colonisation might have predisposed to urinary infection; bacteria in the urine might have seeded on to the vestibule; and finally other factors might have predisposed to infection of both urine and vestibule.

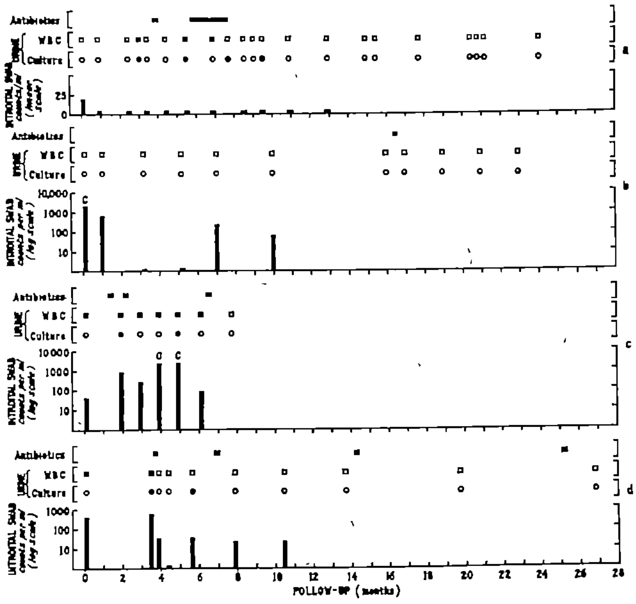

FIG. 3

Patterns of urinary infection in patients from whom serial introital swabs were taken.

(*a*) Two recurrences of *Esch. coli* urine infection occured despite persistently low swab counts.

(*b*) No urine infection occurred despite repeatedly high swab counts.

(*c*) High swab counts were first found in association with an *Esch. coli* infection, and persisted.

(*d*) A high swab count preceded an *Esch. coli* infection, and diminished when this was successfully treated.

Urine Cultures:	○ Not infected ● Infected.
Urine Leucocytes:	☐ < 3 per cu. mm. ● 3-10 per cu. mm. ■ > 10 per cu. mm.
Introital Swabs:	C confluent growth.
Antiobitics:	recorded even if prescribed for infections other than of the urinary tract.

We chose to study this further by considering the prognostic significance of the initial introital swabs, collected when the patients were not receiving antibacterial therapy. Sampling error might be considerable with a swab technique (although this was not suggested by preliminary experiments) and so we considered not only the implication of the first swab obtained, but also that of the first 2 consecutively obtained swabs. Patients from whose introital swabs *Esch. coli* could be cultured were significantly more likely to develop *Esch. coli* urine infections subsequently than patients from whose swabs none could be obtained. It would seem logical that if there are virtually no pathogenic bacteria in the introitus, ascending infection is less likely to occur than if bacteria are plentifully available. However, it was disappointing to find no greater quantitative association between the vestibular flora and the likelihood of infection developing. The data suggests that although the presence of *Esch. coli* in the vestibule constitutes a permissive factor, the development and maintenance of infection in the urine depend more on other factors present in the host.

The prognostic significance of swabs from which *Esch. coli* could be cultured was different from that of swabs from which none could be obtained but the difference was not so great as to make the test an important practical one. The taking of serial swabs might be expected to increase their prognostic accuracy, and it has been suggested that women who persistently carry enterobacteria on their vestibule develop urine infection more often than those who carry them intermittently or not at all (O'Grady, Richards, McSherry, O'Farrell and Cattell, 1970). Nevertheless, analysis of the pattern of infection in patients from whom serial swabs had been taken did not lead to confidence in the practical value of the test. Four such patients are shown in Figure 3, from which it will be seen that urinary infection could occur despite persistently low introital swab counts (Fig. 3*a*), and conversely repeatedly high swab counts did not necessarily predict a future infection (Fig. 3*b*).

We did not consider it feasible to obtain introital swabs from normal women, proved to remain free from urine infection throughout prolonged follow-up. However, Fair, Timothy, Millair and Stamey (1970), using a similar technique to ours, found *Esch. coli* at the introitus of only 3 out of 30 pre-menopausal women who had no history of urinary or vaginal infection, and believed this contrasted sharply with the results of cultures made from women with recurrent urine infections. On the other hand O'Grady *et al.* (1970) found no difference between women with a history of frequency and/or dysuria and women who gave no such history, with regard to the carriage of enterobacteria on the introitus at their first attendance.

Race, age, catamenia, marital status, gravidity, coital frequency, use of contraceptives, menstrual protection, perineal hygiene, and radiological abnormalities of the urinary tract were selected as factors which might quantitatively influence the introital *Esch. coli* flora, or might affect the recurrence of urinary infection independent of this. Patients who develop *Esch. coli* urinary infection during follow-up were found to be significantly older than those who did not do so, and were more often post-menopausal. Otherwise they did not differ from them with regard to these factors.

We could find no evidence that any of the factors studied influenced the vestibular flora to any appreciable extent. Claims that attention to perineal hygiene can influence either vestibular flora or the development of urine infections (Moore and Hira, 1965; Gibbon, 1970) must be regarded as unproven.

SUMMARY

Quantitative cultures from paired introital swab and urine specimens, collected from 191 patients who had a history of recurrent urinary infection, were compared. The introital *Esch. coli* count increased significantly with the urinary count.

In an attempt to establish a causal relationship between introital count and urine infection the prognostic importance of the swab cultures was studied in 83 of the patients whose follow-up satisfied defined criteria. 40·4 per cent of patients from whose first introital swab (taken in the absence of chemotherapy) no *Esch. coli* could be cultured, developed a urine infection due to this organism during follow-up, compared with 66·6 per cent of those from whose swab some *Esch. coli* were obtained. This difference was statistically significant, and its practical relevance is discussed. There was a tendency for infections to occur sooner after swabs from which *Esch. coli* were cultured than after swabs from which they were not, but the difference was not significant.

Some factors considered likely to influence introital flora or the development of urinary infection were studied. Patients who developed *Esch. coli* urine infections during follow-up were significantly older and more often post-menopausal than those who did not do so. However, none of the factors studied appeared to influence quantitatively the introital *Esch. coli* flora.

The results suggest that the availability of *Esch. coli* in the vestibular flora constitutes a

permissive factor for ascending urine infections to occur in women, but thereafter other host factors are of predominant importance.

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NOTICE

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PRE-PROGRAMME 1972

Président du 66 *ème Congrès Francais d'Urologie*: Docteur J. MICHON (Paris)
Vice-Président: Professeur J. DUCASSOU (Marseille)

RAPPORT PRINCIPAL: Lundi, 25 Septembre, 14 heures 30.

Les tumeurs de la voie excrétrice supérieure (calices, bassinets, uretères). Professeur Agrégé E. MAZEMAN, 3 Place de la République, 59 Lille.

Ler FORUM: Mercredi, 27 Septembre, 14 heures 30.

Les résultats des réimplantations de l'uretère dans la vessie.

Animateurs: Professeur R. KUSS, 63 Avenue Niel, Paris 17 ème.
Docteur J. BRUEZIERE, 10 rue de la Pompe, Paris 16 ème.

2 *ème* FORUM: Jeudi, 28 Septembre, 14 heures 30.

Le Priapisme.

Animateur: Professeur AGRÉGÉ L. DURAND, 1 rue Thimonnier, 69 Lyon.

Enquiries should be addressed to the Secretary General: Professor Jean Auvert, 78 Avenue de Suffren, 75, Paris—15e.

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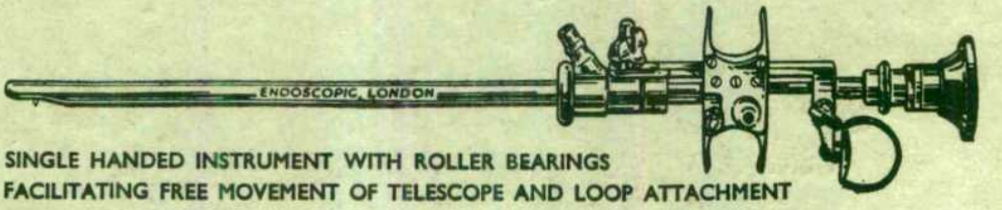

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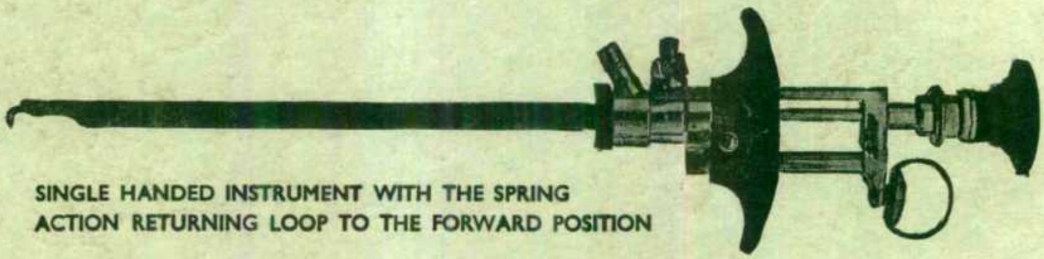

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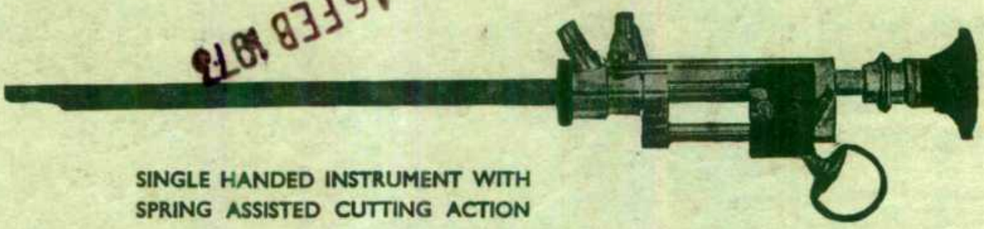

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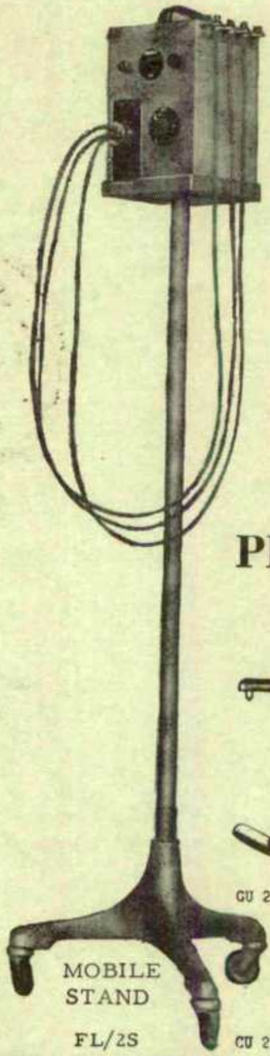

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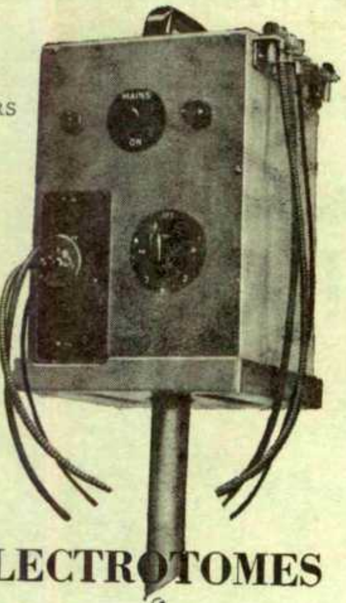

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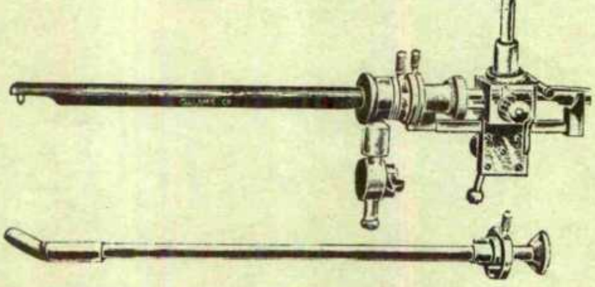

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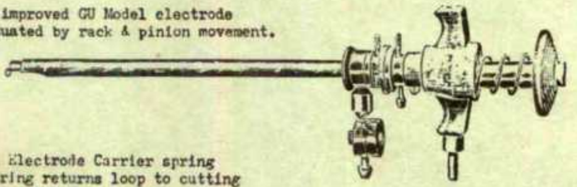

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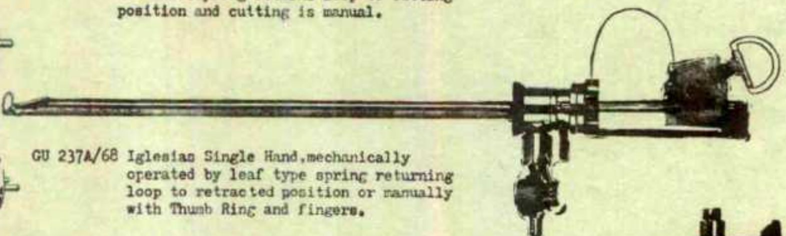

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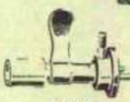

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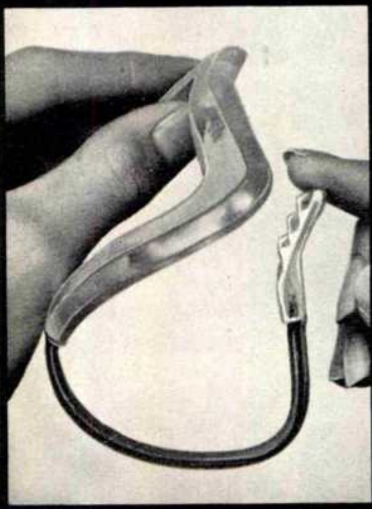

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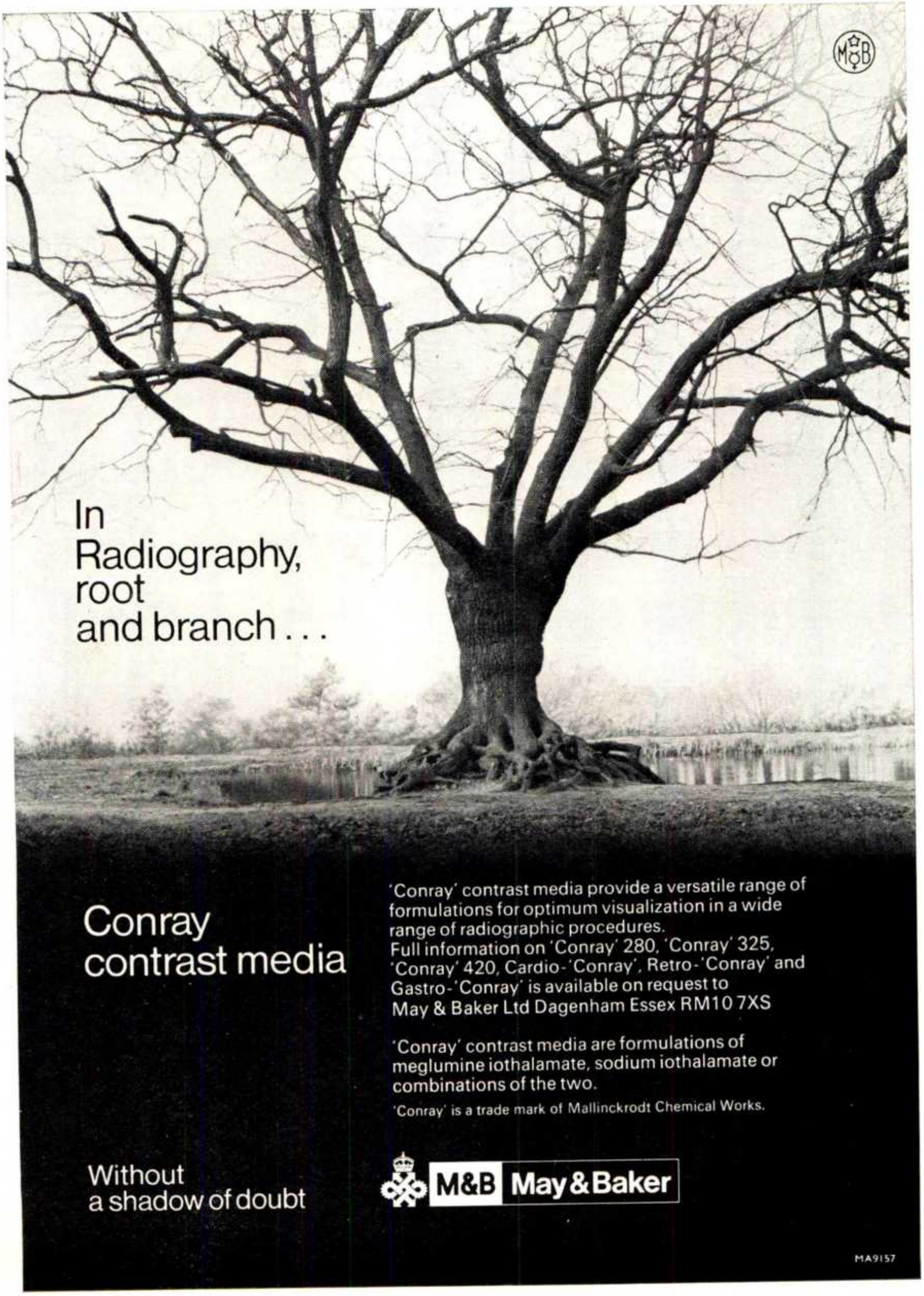

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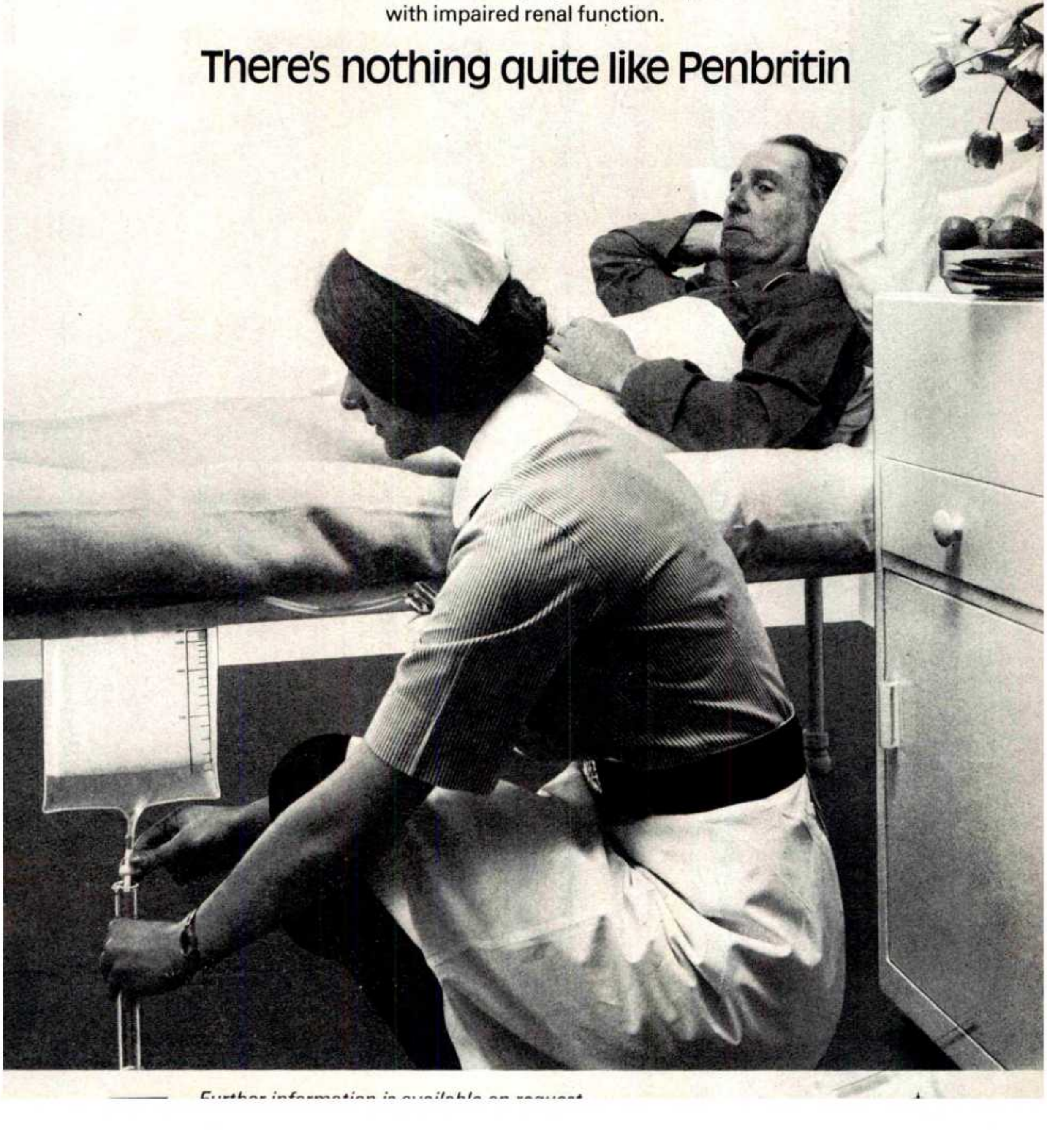

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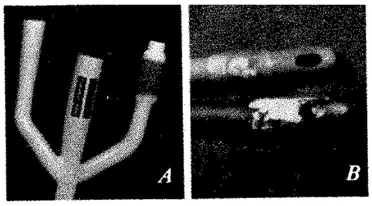

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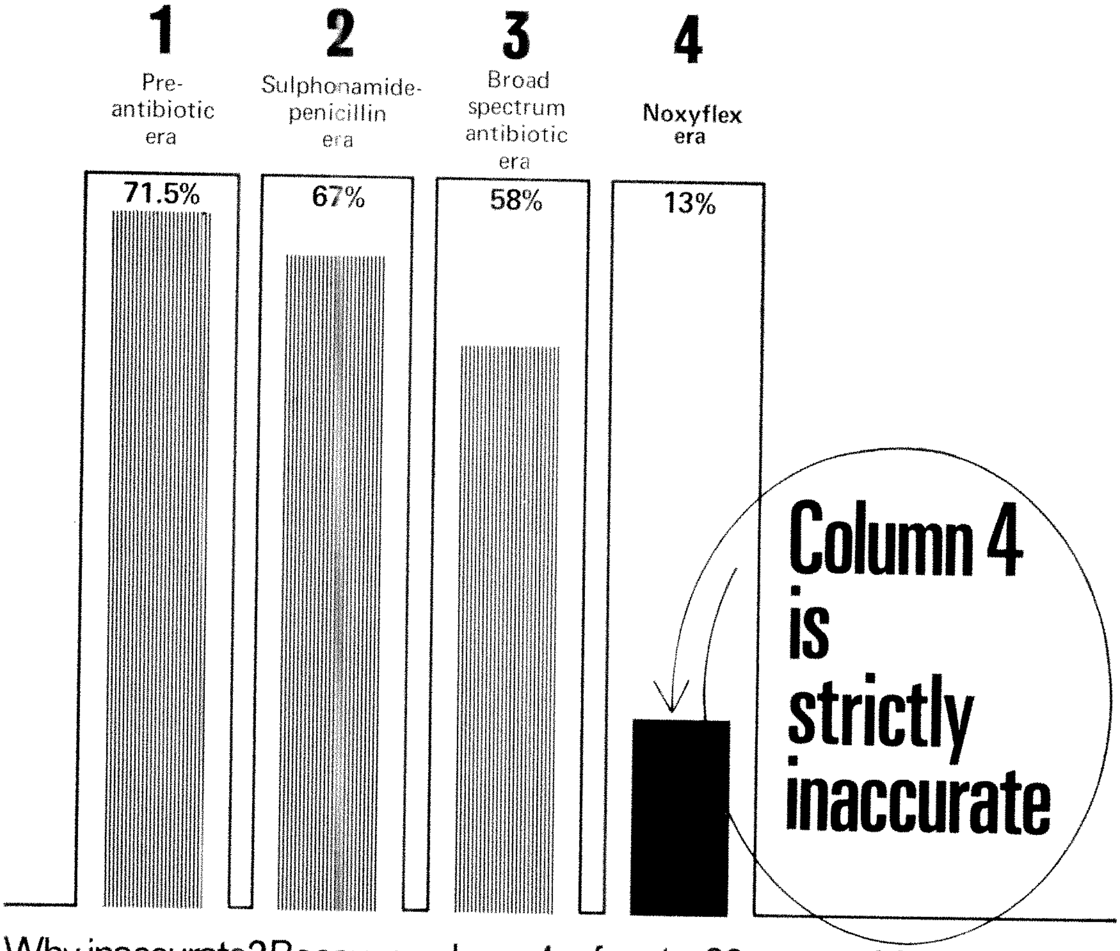

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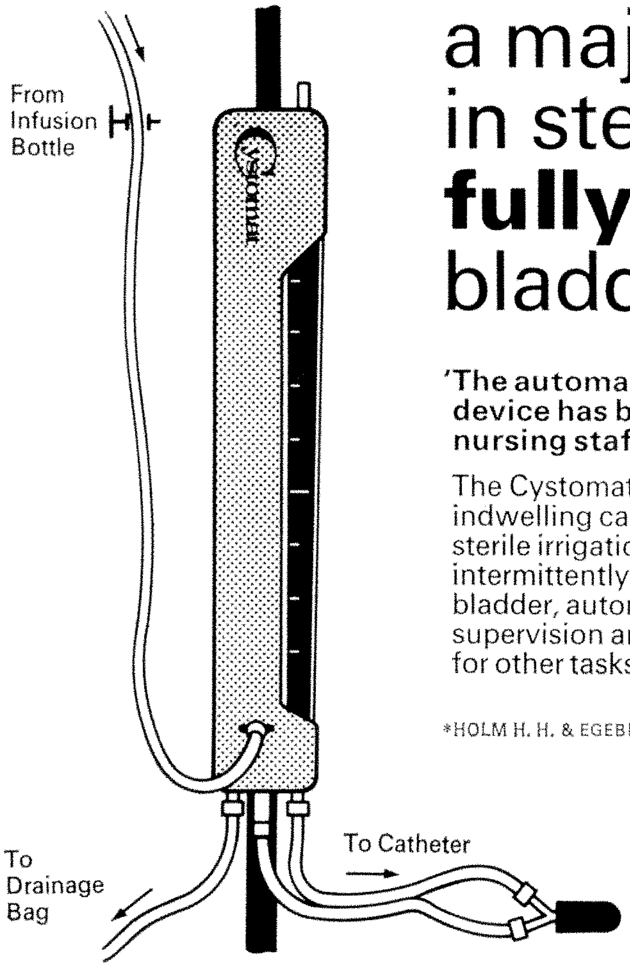

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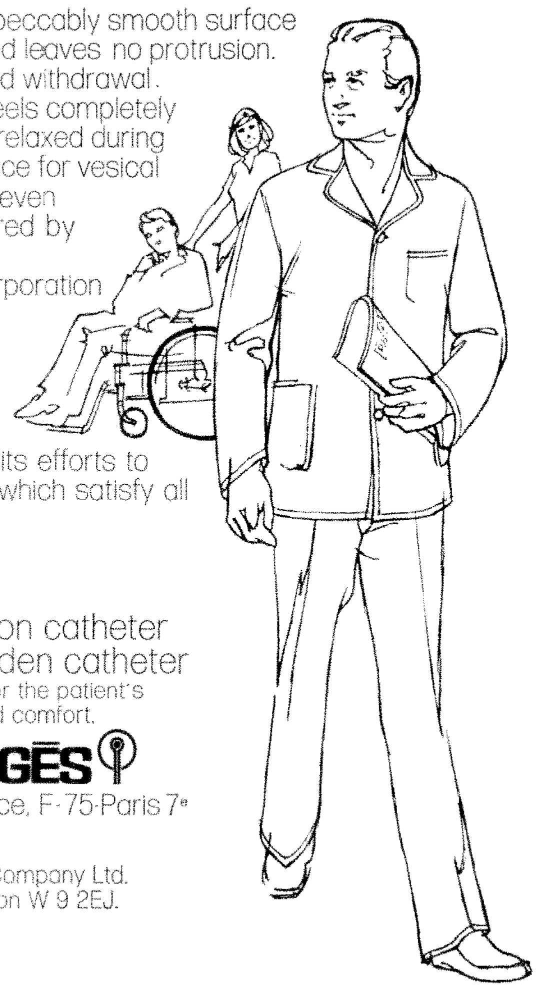

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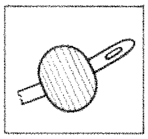

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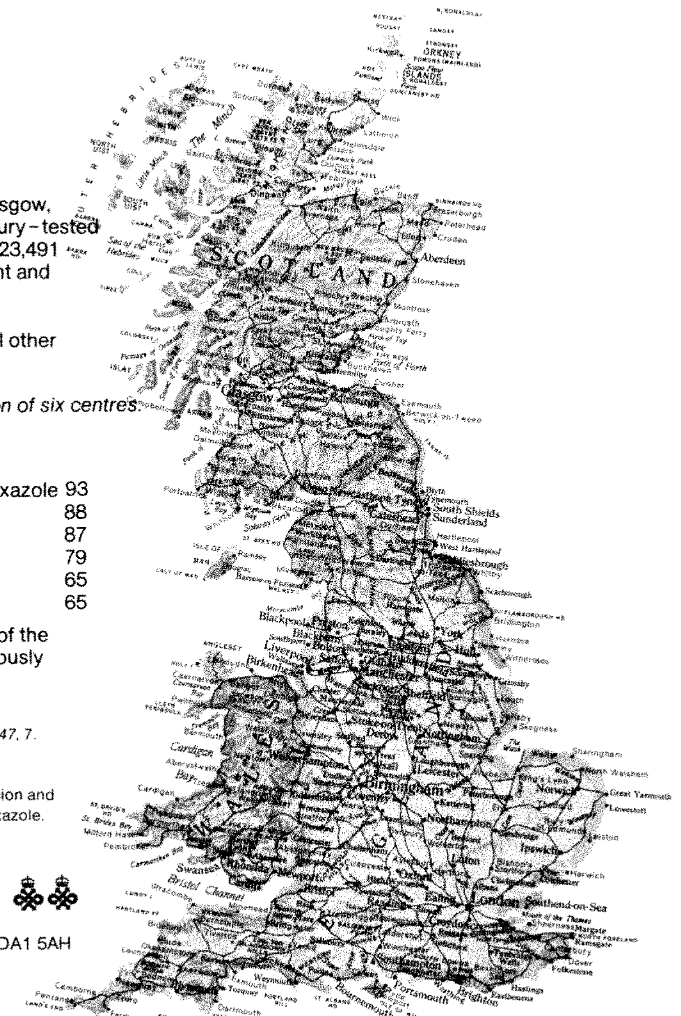

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(1) *Postgrad med J*, (1971), (September Supplement), *47*, 7.
(2) *Brit med J*, (1969) *i*, 541.
(3) Leading Article, *Brit med J*, (1969), *i*, 525.

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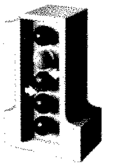

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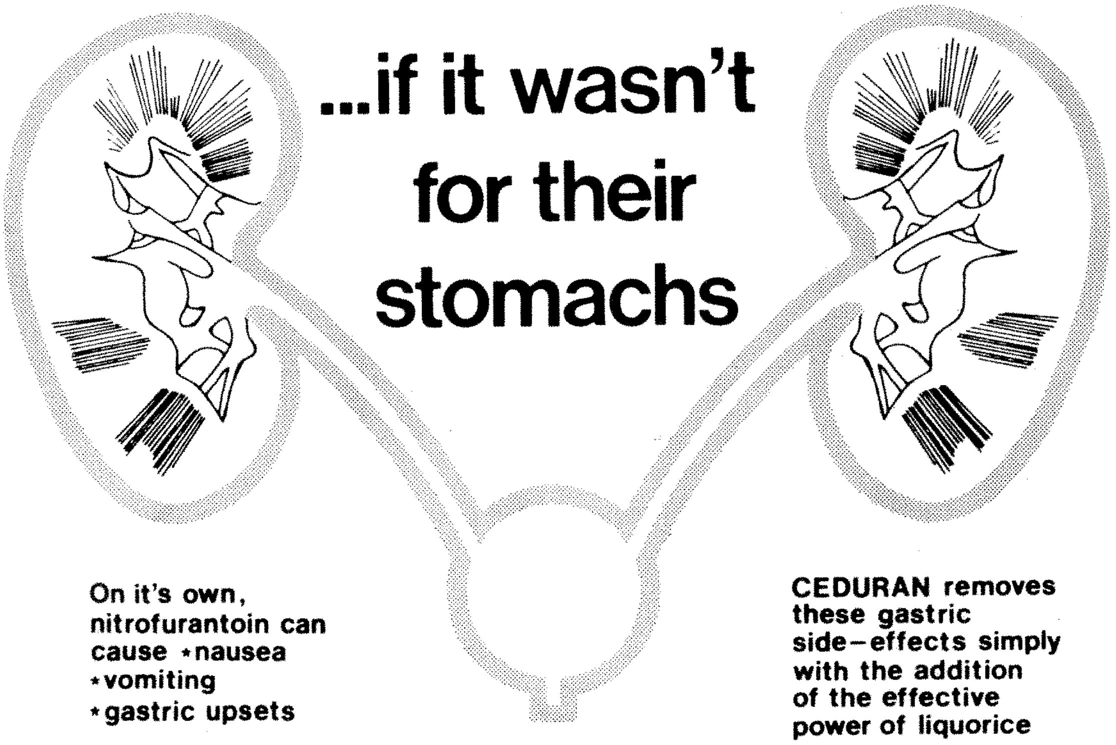

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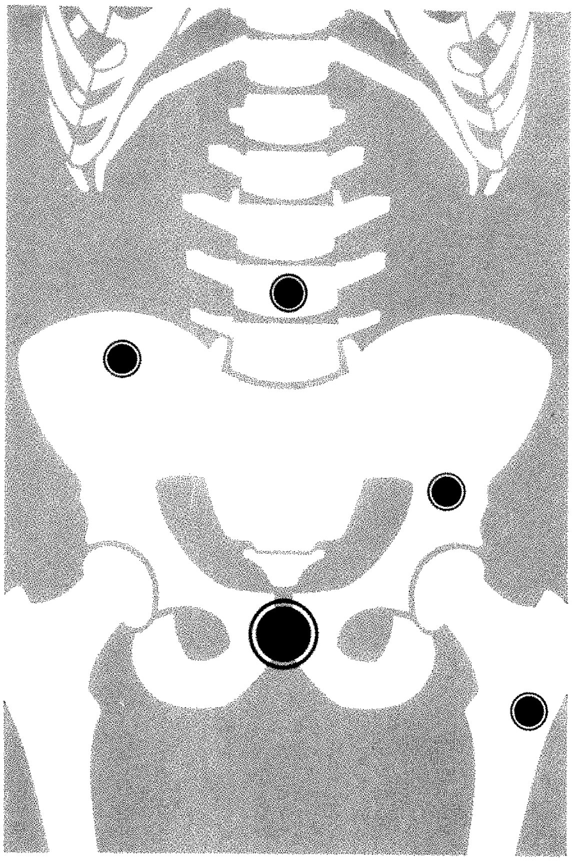

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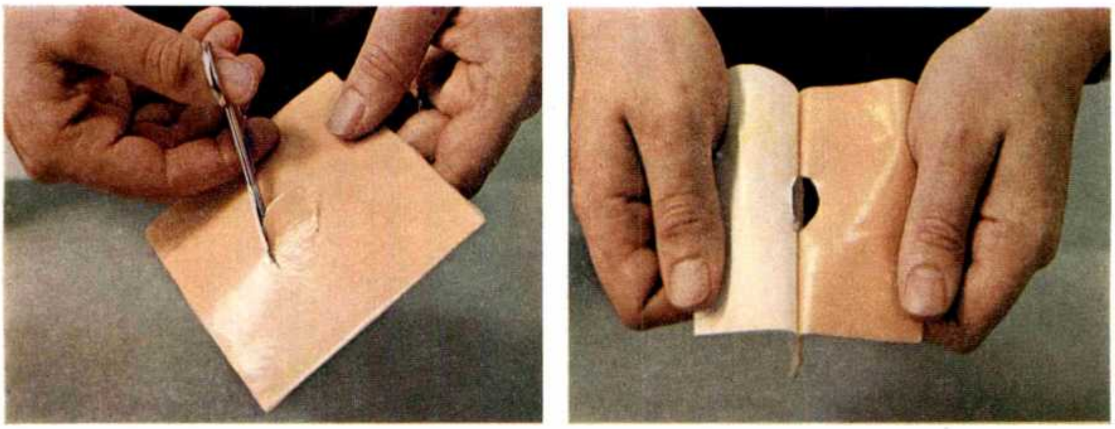

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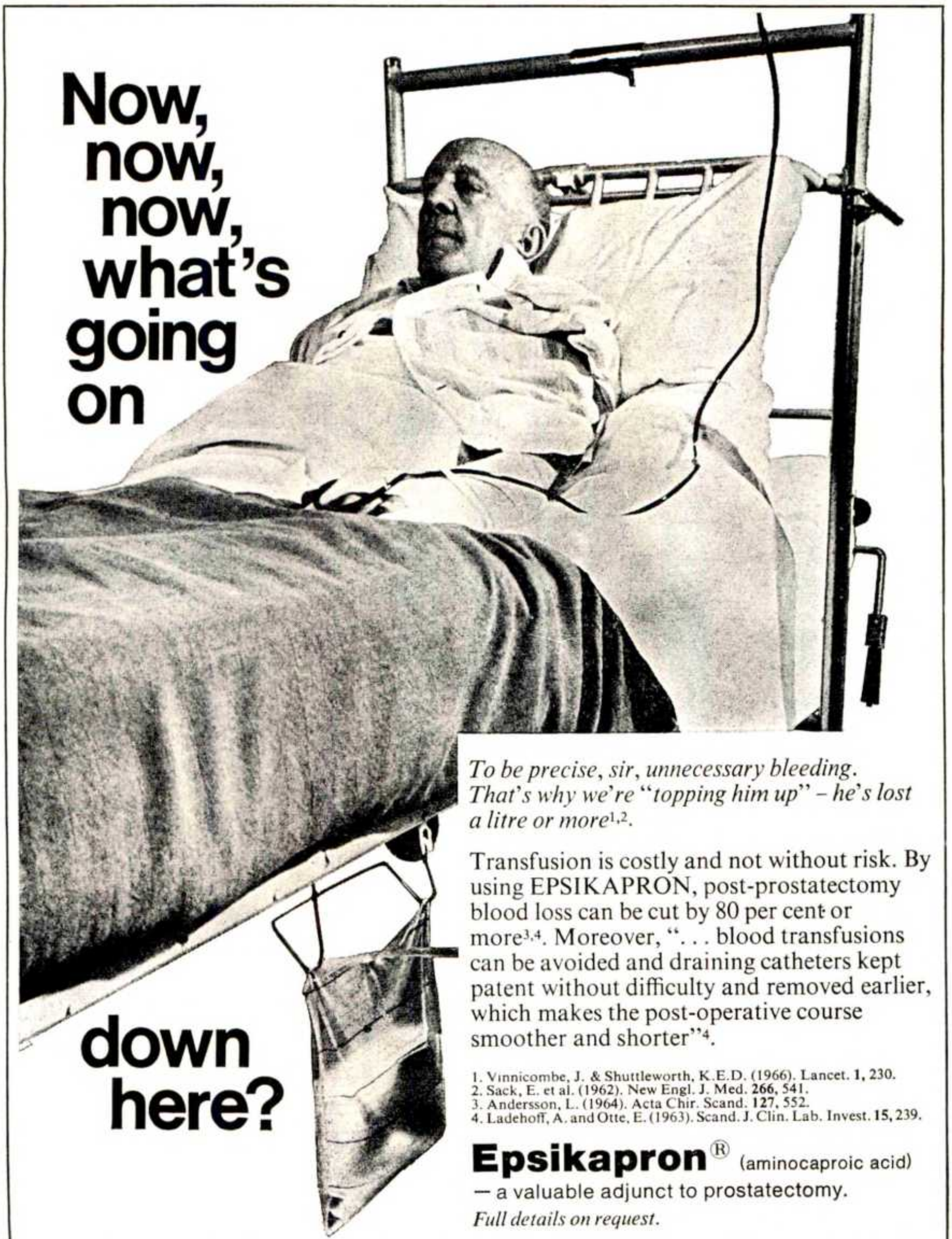

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2. Sack, E. et al. (1962). New Engl. J. Med. **266**, 541.
3. Andersson, L. (1964). Acta Chir. Scand. **127**, 552.
4. Ladehoff, A. and Otte, E. (1963). Scand. J. Clin. Lab. Invest. **15**, 239.

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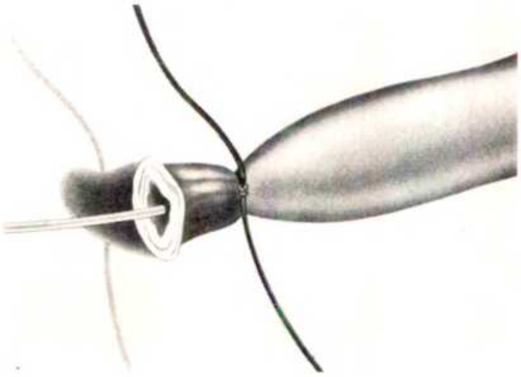

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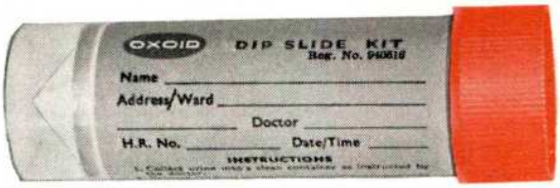

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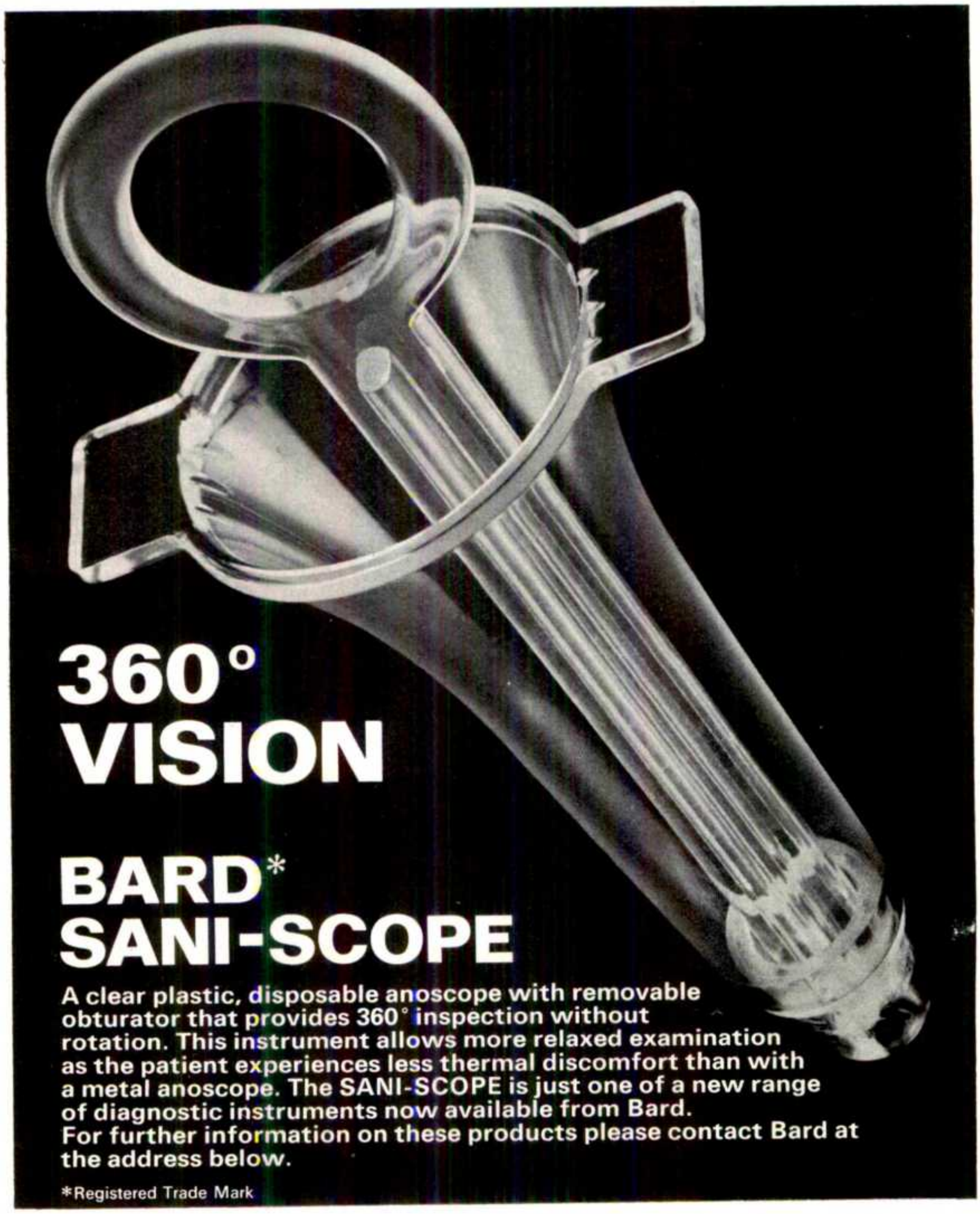

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1. *E.D.T.A. Proceedings*, VOL VI; (1969). 2. *British Journal of Urology*, (1970) **42**; 246. 3. *British Medical Journal*, (1969) **IV**; 717. 4. *British Journal of Urology*, (1970) **42**; 590. 5. *Lancet*, (1963) **ii**; 1143. 6. *J.clin.Path.*, (1964) **17**; 362. 7. Paper presented to the Dutch Ophthalmological Congress, Amsterdam, 1970. 8. *Lancet*,(1970) **ii**; 1116. 9. *J.clin.Path.*,(1964) **17**; 355. 10. *Arch.Dis.Childh.*, (1965) **40**; 235.

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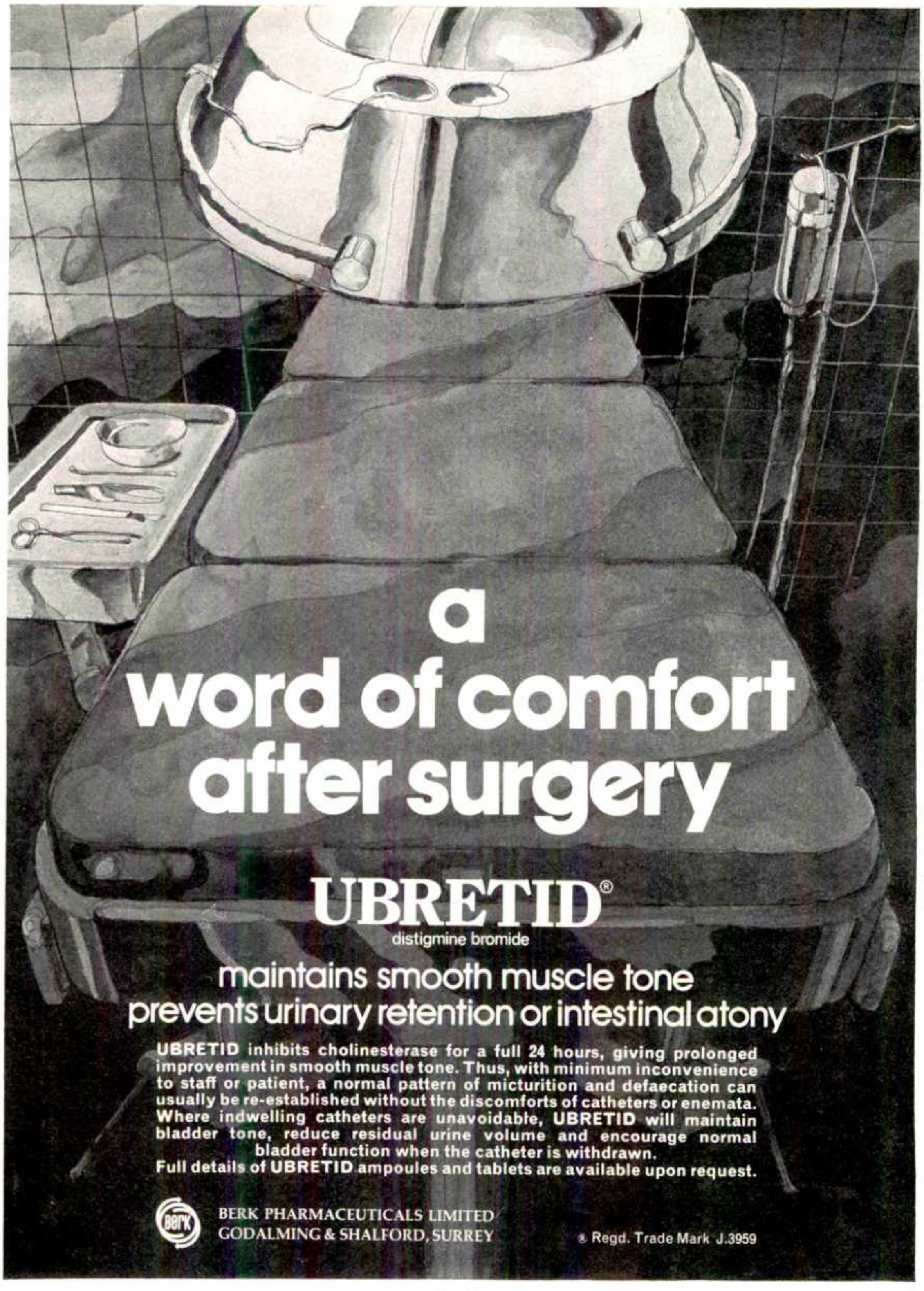

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British Journal of Urology (1972), **44**, 377-383

DONOR KIDNEY SELECTION FOR TRANSPLANTATION

Relationships Between Glomerular Structure, Vascular Supply and Age

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Renal senescence in man is believed to result from alterations in the renal arterial system which is part of the process occurring generally throughout the vascular system with advancing years (Oliver, 1952). Its progress is hastened by the presence of hypertension (Heptinstall, 1966). The resulting narrowing and decrease in the number of the renal vascular pathways and associated vasoconstriction cause gradual diminution in renal function (Davies and Shock, 1950) and ischæmic obsolescence of renal glomeruli (McManus and Lupton, 1960).

Because of their large reserve, kidneys are rarely exhausted to a point of appreciable decompensation to be a cause of death in old age. Until the advent of renal transplantation the biological problem of the ageing of the kidney was mainly of theoretical interest only.

The present investigation was undertaken to re-evaluate senescent changes in the kidneys particularly in relation to arterial changes and glomerular obsolescence with the aim of determining an age beyond which persons should best not be considered as kidney donors.

Material and Methods.—Kidneys from 50 consecutive necropsies were examined macroscopically and microscopically to assess and compare glomerular appearance, vascular changes and renal artery circumference. Correlation was made also with previous history of hypertension.

The kidneys were weighed and minimum circumference of the main renal arteries measured with dividers and ruler. Two blocks were taken from each kidney. Sections were prepared and stained by hæmatoxylin and eosin, periodic acid-Schiffs/alcian blue, Masson trichrome and Verhoeff-Van Gieson. Kidneys showing renal parenchymal disease, *e.g.*, pyelonephritis, glomerulonephritis, were excluded from further study but not those showing sclerotic vascular changes only. For each of the remaining kidneys glomeruli were examined and graded as normal, completely obsolescent or intermediate if the sclerotic changes present did not amount to complete obsolescence.

Vascular, tubular and interstitial changes were graded. The large renal arteries were graded 0 (none) to 3 (severe) on the degree of intimal abnormality (thickening, fibrosis, elastosis, new muscle and fibrin) and 0 (none) to 3 (severe) on the degree of medial abnormality (thinning, loss of muscle and fibrosis). The arterioles were graded 0 (none) to 4 (severe extensive) on the presence and extent of hyalinisation.

Tubular atrophy was graded 1-3 (scattered 1, focal 2, generalised 3) while interstitial fibrosis was graded 1 minimal focal to 3 severe generalised.

RESULTS

Out of the 50 pairs of kidneys examined, 9 pairs were excluded from further study because of the presence of renal parenchymal disease (diabetic nephropathy 3 cases, chronic sclerosing glomerulonephritis 3 cases, chronic pyelonephritis 2 cases, and 1 case of end stage kidney with malignant hypertensive changes). The causes of death in the remaining 41 patients are shown in Table I. The age range of these patients was 28-89 years with a mean of 65 years (S.D. 10). There were 22 males and 19 females. Significant correlation was found between age and the probits of the percentage of completely normal glomeruli ($r = -0{\cdot}6$, Fig. 1). The regression line

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TABLE I

Causes of Death in the Remaining 41 Patients

Cardiovascular (14)	
Myocardial infarction	9
Ischæmic heart disease	3
Valvular disease	2
Respiratory (11)	
Bronchopneumonia	4
Pulmonary embolism	4
Carcinoma of the bronchus	2
Restrictive lung disease	1
Central nervous system (7)	
Cerebral hæmorrhage	5
Cerebral glioma	1
Disseminated sclerosis	1
Gastro-intestinal (4)	
Colonic diverticular disease	2
Duodenal ulcer	1
Crohn's disease	1
Liver (3)	
Cirrhosis	3
Pancreas (2)	
Acute pancreatitis	1
Chronic pancreatitis	1

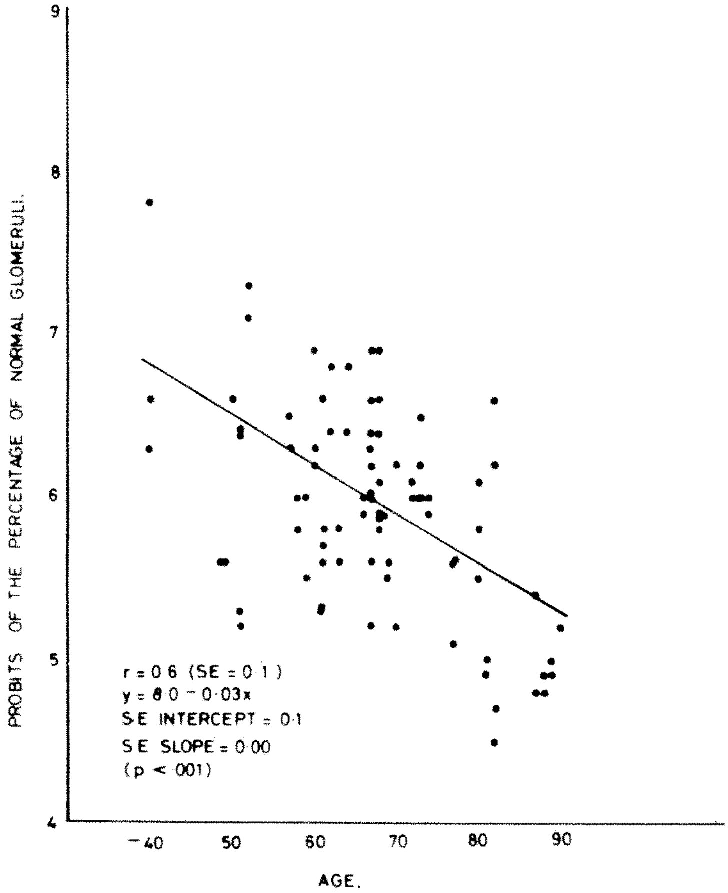

FIG. 1

The relationship between the probits of the percentage of normal glomeruli and age.

drops from the equivalent of 95 per cent normal glomeruli up to the age of 40 years to 63 per cent at 90 years.

There was also correlation between the minimum renal artery circumference and the percentage of normal glomeruli (*r* = 0·36, Fig. 2). The narrower the internal circumference the lower the proportion of normal glomeruli. (One kidney with two renal arteries was excluded from this correlation.) With an internal renal artery circumference of less than 10 mm. there were no kidneys with 90 per cent or more normal glomeruli. The proportion of kidneys with 90 per cent or more completely normal glomeruli progressively increased to $\frac{25}{77}$ for kidneys less than 17 mm. renal artery circumference. The percentage agreements and selection proportions were determined by comparing the percentage of normal glomeruli cut-off points with 10-year period age steps (Table II) and renal artery circumferences in 2 mm. steps (Table III). If greater than 60 per cent completely normal glomeruli and less than 80 years were taken as cut-off points the percentage agreement was 90 per cent and selection proportion $\frac{4}{5}$, *i.e.*, 4 false positives and 5 false negatives. If greater than 50 per cent was taken as the cut-off point at the same age there were still 5 false negatives but no false positives. If however 90 per cent or more completely normal glomeruli were required the percentage of such kidneys varied from 67 per cent at less than 50 years to 8 per cent from subjects older than 70 years (Fig. 3). With regard to minimum renal artery circumference (Table III), if greater than 60 per cent completely normal glomeruli

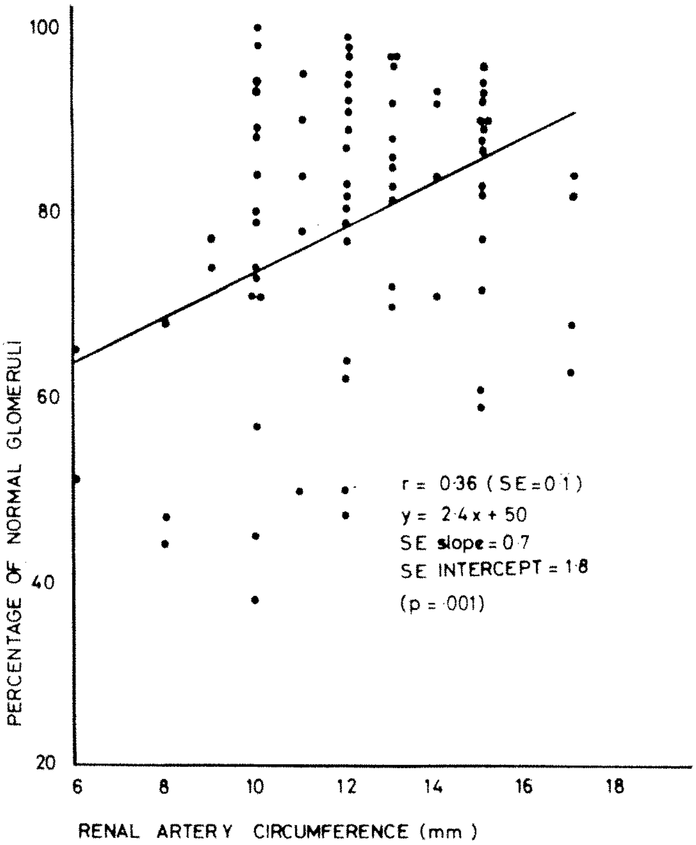

FIG. 2

The relationship between the percentage of normal glomeruli and renal artery circumference.

TABLE II

Percentage Agreements and Selection Proportions[1]

Age cut-off points	Percentage Normal Glomeruli Cut-off Points				
	>90%	>80%	>70%	>60%	>50%
<50	69% 2/23	40% 2/47	29% 0/58	23% 0/63	15% 0/69
<60	71% 11/13	54% 5/32	45% 2/43	40% 1/48	36% 0/53
<70	56% 33/2	62% 19/12	74% 7/14	79% 2/15	79% 0/17
<80	41% 47/1	67% 23/4	84% 9/4	90% 4/5	93% 0/5

(The standard errors of the agreements varied from 2 to 5%.)

[1] Selection proportion $= \dfrac{\text{false positives}}{\text{false negatives}}$ (c/b).

If an arbitrary age limit cut-off is taken:
c = Kidneys *without* the necessary percentage of normal glomeruli.
b = Kidneys with the necessary percentage of normal glomeruli excluded.

TABLE III

Percentage Agreements and Selection Proportions[1]

Renal artery circumference cut-off points (mm.)	Percentage Normal Glomeruli Cut-off Points				
	>90%	>80%	>70%	>60%	>50%
>6	30% 57/0	60% 32/0	79% 17/0	86% 10/1	88% 8/2
>8	33% 54/0	64% 29/0	81% 13/2	88% 8/2	89% 6/3
>10	47% 39/4	69% 18/7	69% 10/15	73% 4/17	69% 3/19
>12	56% 24/12	62% 9/22	53% 5/33	53% 1/37	52% 0/39
>14	59% 15/18	50% 6/34	36% 4/48	35% 1/52	33% 0/54
>16	68% 4/22	34% 2/45	25% 2/51	18% 0/66	15% 0/69

(Standard errors of agreements varied from 3 to 6%)

[1] Selection proportion $= \dfrac{\text{false positives}}{\text{false negatives}}$ (c/b).

If an arbitrary renal artery circumference cut-off is taken:
c = Number of kidneys without the necessary percentage of normal glomeruli.
b = Number of kidneys with the necessary percentage of normal glomeruli excluded.

was again taken as a cut-off point the number of false positives decreased with increasing cut-off point of renal artery circumference but the number of false negatives increased while the percentage agreement declined.

In 28 of the 41 patients recordings of blood pressure were available. Readings immediately prior to death were excluded because they were unreliable due to the terminal condition. There was no significant difference between the percentage of normal glomeruli in patients with previous diastolic blood pressure above or below 100 mm. Hg. in the range examined.

Significant correlation between age and total muscular artery abnormality ($r = 0{\cdot}6$) was found while correlation of age with arteriolar change was just significant ($r = 0{\cdot}24$) and there was no significant correlation between age and renal artery circumference.

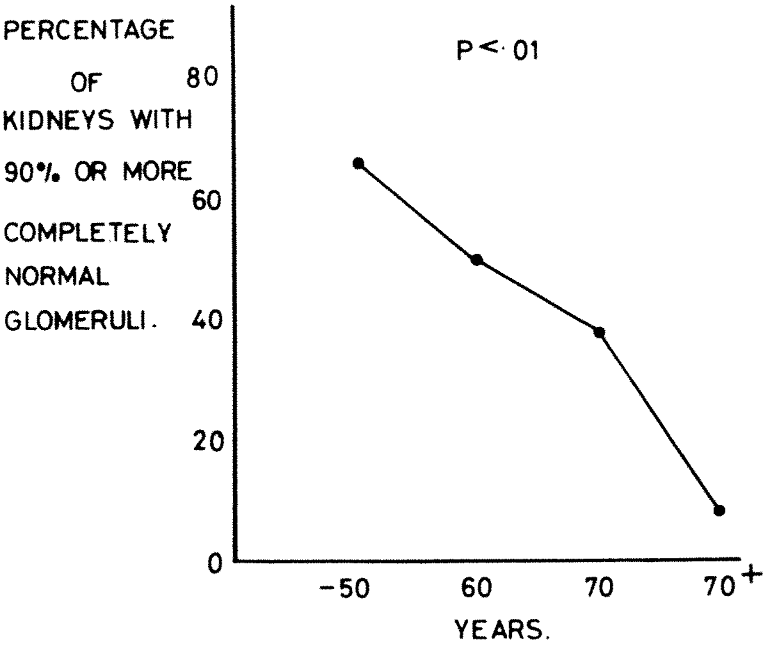

FIG. 3

The relationship between the percentage of kidneys with 90 per cent or more completely normal glomeruli and age.

The gross renal weights (x) significantly correlated with minimum internal renal artery circumference (y) ($r = 0{\cdot}43 : y = 8{\cdot}3 + 0{\cdot}3x$) and in the 52 cases in which it was measured with pole to pole measurements (y) ($r = 0{\cdot}6 : y = 75 + 0{\cdot}24x$).

A significant negative correlation between the percentage of normal glomeruli and total tubular artophy ($r = -0{\cdot}5$) was found but there was no significant correlation with grades of interstitial fibrosis.

DISCUSSION

The results in this series indicate that if kidneys with 90 per cent or more completely normal glomeruli are required it would seem best to use as donors persons of 50 years of age or less. However, if lower levels of percentage normal glomeruli are considered adequate, kidneys from older persons can be found to meet requirements as indicated (Table II).

The correlations between the minimum renal artery circumference, the percentage of normal glomeruli and renal weight are of interest in view of the relationship between the radius of the renal artery, effective renal blood flow, inulin and PAH clearance as shown by Ofstad, Gjersvik and Kolsaker (1969) in patients with renal parenchymal disease. Reduction of these functional parameters with increasing age was demonstrated by Dixon and Shock (1950).

The level of diastolic blood pressure was not statistically related to the percentage of normal glomeruli in this series. This is perhaps explicable if one considers glomerular obsolescence as a dynamic process (McManus and Lupton, 1960), secondary to vascular changes which themselves result from the raised blood pressure. It was not, however, possible to obtain accurate data of the length of hypertensive history in this series.

The correlation between the percentage of normal glomeruli and degree of tubular atrophy is of interest in the light of renal biopsies examined by Striker *et al.* (1970) who demonstrated that total glomerular change correlated well with interstitial and tubular abnormalities. Schainuck *et al.* (1970), analysing functional changes in the same series, showed that regardless of the basic disease in the kidney the impaired renal function was most closely related to change in the tubules or interstitium. It is perhaps this factor together with diminished regenerative capacity of tubular epithelium with age (MacKay *et al.*, 1932) which may prove more important than moderate glomerular abnormality in the use of ageing kidneys for transplantation purposes.

There were 3 cases of diabetic nephropathy in this series in known diabetics. They were all over 50 years of age and the duration of the disease was not known. Seven other diabetics in this series, mean age 68 (range 61 to 74) showed no evidence of diabetic nephropathy. MacDonald and Ireland (1964) have shown that some insulin dependent diabetics of more than 20 years' standing have no significant involvement on light and electron microscopy, but Birkman and Rifkin (1966) regarded the duration of the diabetes to be the single most important factor in determining the severity of the nephropathy. The results suggest that care is necessary in selection of donor kidneys for transplantation purposes from diabetic patients and that if the disease has been present for a prolonged period their use is best avoided.

SUMMARY AND CONCLUSIONS

Kidneys from 50 consecutive post-mortems were examined macroscopically and histologically to assess and compare glomerular appearance, vascular changes and renal artery circumference. The aim of the investigation was to determine the age beyond which persons, without obvious renal parenchymal disease, should best not be considered as kidney donors. Out of 100 kidneys 82 were used for the study, 18 were excluded because of renal parenchymal disease. Glomeruli were graded as normal, obsolescent or intermediate.

Significant correlations between age, renal artery circumference and the percentage of normal glomeruli were found.

If kidneys with 90 per cent or more completely normal glomeruli are required it would seem best to use as donors persons of 50 years of age or less, however, if lower levels of percentage normal glomeruli are considered adequate, kidneys from older donors can be found to meet requirements. In fact all the kidneys with no obvious renal parenchymal disease in this series from persons less than 80 years of age possessed more than 50 per cent of apparently completely normal glomeruli.

There was no significant difference between the percentage of normal glomeruli in patients with previous diastolic blood pressures above or below 100 mm. Hg in the range examined. The danger of using donor kidneys from known diabetics is discussed. The minimum circumference of the main renal artery was found to give a useful measure of the percentage of normal glomeruli.

We are indebted to Dr R. A. Dixon for helpful advice in regard to statistical analysis of our data.

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VESICO-URETERIC REFLUX AFTER RENAL TRANSPLANTATION

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The ureteric complications of renal transplantation have been discussed at length in several recent papers by Owen (1972), Rees (1972) and Robson and Calne (1971). There has been a review of ureterovesical competence following renal transplantation by Powis, Barnes and Dawson Edwards (1971).

Micturating cysto-urethrography and excretion urography were performed on 21 patients following cadaveric renal transplantations. Ureterovesical competence was thus assessed at 24 anastomoses since 1 donor kidney had a double ureter and 2 patients had a second renal transplantation. No complications or infection resulted from these investigations.

The average period of clinical follow-up was 2 years, 2 months (6 months-4 years). Radiological follow-up is defined as the time between renal transplantation and the last relevant film. In this study it was 1 year 3 months (6 months-3½ years) since excretion urography was carried out only when required on clinical grounds and micturating cysto-urethrography was not repeated.

Methods.—Three basic methods of ureteric re-implantation were employed.

In Group 1, totalling 15 re-implantations, a tunnelling technique was used giving an oblique course through the bladder wall together with a sub-epithelial portion of intravesical ureter. In some cases a nipple was fashioned, whilst in others the ureteric orifice was anastomosed to the epithelium of the bladder. A ureteric splint was sometimes employed but this did not affect the basic technique. The 15 operations were carried out by a total of 4 surgeons.

Group 2 utilised the redivac drain introducer. The catheterised ureter was threaded on to the introducer and then stabbed obliquely through the bladder wall, the ureter being tacked to the bladder epithelium. These operations were carried out by 2 surgeons.

In Group 3 a miscellany of methods was used. In 1 instance a short ureter was anastomosed directly to the bladder epithelium and in 2 further instances reconstructions were carried out using the Psoas Hitch or Boari Flap to anastomose the bladder direct to the renal pelvis.

RESULTS

(Table).

In Group 1, using the tunnel technique, only 1 case out of 15 showed ureterovesical reflux into the transplanted kidney. Two cases showed reflux into their own ureters but not into the transplanted ureter.

In Group 2 using the stab technique 5 of the 6 cases showed reflux into the transplanted kidney. One of these also refluxed into her own ureters.

In Group 3, where direct ureterovesical anastomosis or reconstruction without any anti-reflux procedure had been carried out, all refluxed as predicted.

No case of distal ureteric obstruction was seen in any group.

DISCUSSION

Routine bacteriological follow-up examinations of the urine confirmed that the presence of vesico-ureteric reflux either into the recipient's own ureter or into the transplanted ureter favoured the persistence of urinary infection albeit controlled by antibiotics. The significance of the

GROUP 1.	TUNNEL IMPLANTATION		15
	REFLUX	1	
	COMPETENT	14	
GROUP 2.	STAB WITH REDIVAC INTRODUCER		6
	REFLUX	5	
	COMPETENT	1	
GROUP 3.	OTHERS		3
	REFLUX	3	
	COMPETENT	0	

Table

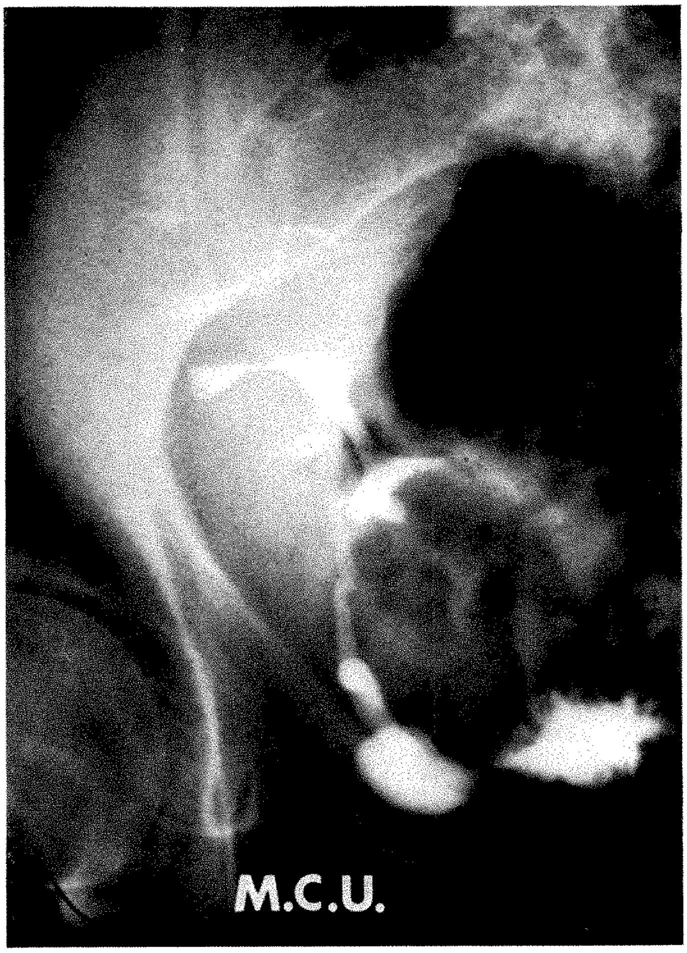

Fig.

reflux of infected urine has been clearly indicated in other papers (Williams and Porter, 1966) and no further discussion of this aspect is required.

In the solitary case where failure occurred amongst the 15 cases in Group 1, a perivesical diverticulum is seen on the micturating cystogram (Fig.) and the excretory urogram shows that the ureter is implanted into the diverticulum. This herniation of epithelium probably occurred due to slight tension on the anastomosis and/or a failure to anchor the ureter to the bladder with an adequate bite of the bladder musculature.

The stab technique represents a superficially attractive method of re-implantation particularly economical of the operator's time and yet, judged by results in the hands of 2 surgeons, fundamentally unsound. Possibly the intravesical portion of the ureter sloughs back to the muscle tunnel as when it is implanted directly through the bladder wall leaving no intravesical ureter.

Predictably the third group refluxed and they are not discussed further.

The investigations of Powis, Barnes and Dawson Edwards (1971) showed that 8 out of 18 cases refluxed following a tunnel type of re-implantation and perhaps suggested that there may be a special problem associated with ureteric re-implantations following transplantation. However our studies do not support such a hypothesis.

CONCLUSION

We conclude as follows:

The tunnel technique has given satisfactory results in this series in the hands of several surgeons. The stab technique utilising the redivac drain introducer should be abandoned. No special problem is associated with ureteric re-implantation following cadaveric renal homotransplantation, assuming a satisfactory vascular supply to the lower ureter is re-established.

We thank Mr David Crosby and Mr John Salaman for allowing us to study their cases, Dr Max Sussman for his help with the bacteriology and Miss S. Robins for secretarial assistance.

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OXYMETHOLONE IN THE TREATMENT OF ANÆMIA IN CHRONIC RENAL FAILURE

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Blood transfusion, once the standard treatment of anæmia in chronic renal failure, is now withheld whenever possible to avert hepatitis and sensitisation against subsequent renal transplant. The great majority of patients on conservative treatment can maintain an acceptable hæmatocrit until their uræmia is so advanced that they require dialysis or transplantation. After the start of regular hæmodialysis, however, the anæmia is aggravated by red cell damage in the extracorporeal circuit and by numerous external losses—residual blood in the dialyser, blood sampling for biochemical control, bleeding from fistula needling sites or at declotting operations, menorrhagia from anticoagulants and technical accidents such as leakage from, or clotting in, the dialyser. The first patients at Seattle required 3-5 pints of blood per month to replace these losses and maintain hæmatocrits of 18-24 per cent (Hegstrom *et al.*, 1962). Transfusion requirements fell with better dialyser design and economy in investigation and by 1967 doctors at 3 English centres had instituted a " no-transfusion " policy (Crockett *et al.*, 1967; Verroust *et al.*, 1967). Their patients often sustained an initial fall in hæmatocrit to 12-15 per cent but about 90 per cent of them could tolerate this trough and subsequently experienced a spontaneous rise in hæmatocrit.

The no-transfusion policy was readily accepted by others but difficult to implement. By 1969, 13 per cent of European teams were still transfusing routinely, 67 per cent found it necessary to transfuse from time to time for symptoms and only 20 per cent used transfusion for emergency only (Drukker *et al.*, 1969). Although we classified ourselves in the last group, the term " emergency " was interpreted liberally since our patients without routine transfusion maintained an average hæmatocrit of only 20 per cent and a minor accident like the loss of 300 ml. of blood in a clotted dialyser often necessitated a transfusion. A drug which could raise the average hæmatocrit by as little as 5 per cent would make a big contribution to rehabilitation and eliminate the need for most of our emergency transfusions. Androgens and related steroids stimulate erythropoiesis in hypoplastic anæmias and by 1969 there were preliminary reports that one such drug (fluoxymetholone) was sometimes effective in the anæmia of renal failure (Eschbach and Finch, 1970; Shaldon *et al.*, 1970). These studies were uncontrolled but sufficiently promising to justify a controlled trial in patients on regular hæmodialysis. From the available drugs we selected oxymetholone since it had been used with outstanding success in hypoplastic anæmia (Allen *et al.*, 1968; Silink and Firkin, 1968; McCredie, 1969; Sanchez-Medal *et al.*, 1969) and had comparatively little masculinising effect.

Materials and Methods.—Fifty-five patients who had been treated by regular hæmodialysis for periods of a few weeks to over 5 years agreed to enter the trial. Each acted as his own control but half the patients started on oxymetholone 100 mg. daily and the other half on placebo to eliminate any bias due to the sequential changes in hæmatocrit described in the introduction. Since our home patients were receiving 3 dialyses (of 10 hours) per week and the hospital patients only 2 (of 12 to 14 hours) these were evenly divided between the 2 groups; the 8 anephric patients were assigned in the same manner. We anticipated that a uniform double blind code would rapidly become ineffective if female patients developed masculinisation which might bias the recording of side effects. Each patient was therefore coded separately by Dr Moore-Robinson and the codes broken only at the final analysis. Pill boxes were returned to check that the correct dose had been taken.

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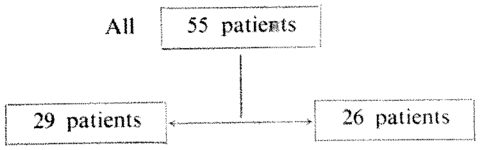
In order to give the drug every chance of success it was necessary to eliminate any deficiencies of the essential factors of which patients on regular dialysis are sometimes depleted by blood loss, dietary restriction or diffusion through the dialyser—iron, folate, pyridoxine and vitamin C (Hampers *et al.*, 1967; Lawson *et al.*, 1968; Mackenzie *et al.*, 1968; Wright *et al.*, 1968; Siddiqui *et al.*, 1970). Consequently patients were given large supplements of these plus other B vitamins for one month before the trial and smaller supplements during the trial (Table I).

TABLE I

Protocol of Trial on Patients undergoing regular Hæmodialysis

First 4 weeks: 55 patients
  Daily supplement of:
    Ferrous sulphate 360 mg.
    Folic acid 15 mg.
    Pyridoxine 25 mg.
    Ascorbic acid 300 mg. (with mixed B vitamins as Allbee with C)
  Single injection of cyanacobalamin 500 μg.

Following 6 calendar months:



Ferrous sulphate 180 mg. daily
Folic acid 5 mg. daily
Pyridoxine 5 p mg. daily
Ascorbic acid 300 mg. (as Allbee with C)

Placebo 3 months
Oxymetholone 3 months
100 mg./day

Oxymetholone 100 mg./day 3 months
Placebo 3 months

Investigations throughout:
  Hb, PCV every 2 weeks
  Symptom questionnaire every 2 weeks
  Limited liver function tests every month

Patients were asked to complete a fortnightly questionnaire which listed 40 possible symptoms, some typical of uræmia, some common side effects of androgen therapy. Limited liver function tests were carried out monthly since oxymetholone is a 17-substituted steroid which may cause jaundice.

A pilot trial of oxymetholone was conducted in 5 patients with normochromic anæmia due to chronic renal failure who were still on conservative treatment. All were given no treatment for a control period of several months then oxymetholone 50 mg. twice daily for a further period of several months; serum bilirubin, flocculation tests, glutamic-oxaloacetic transaminase, proteins, electrophoresis and alkaline phosphatase were checked monthly.

RESULTS

Patients on Regular Hæmodialysis.—(1) *Effect of Preliminary Vitamin Supplements.*—Only 2 patients showed any appreciable change in Hb during the pre-trial month of vitamin therapy. The rises were from 5·2 to 9·3 and 6·1 to 8·9 g./100 ml. respectively.

(2) *Effect of Oxymetholone on the Hb Level and Hæmatocrit.*—Of the 55 patients who started the trial, 16 dropped out for the reasons listed in Table II. The 4 deaths were evenly divided between patients taking oxymetholone and those taking placebo pills at the time and none appeared to be related to therapy.

Of the remaining 39, 22 completed the trial according to the protocol in Table I. Seventeen had completed 4½ months of the trial when this was terminated for administrative convenience at a time when inspection of the coded results suggested that no patient had received any benefit from treatment. The times of exposure to oxymetholone and placebo therapy are shown in Table III. The mean changes in hæmoglobin and hæmatocrit are shown in Table IV; there was no significant difference between oxymetholone and placebo. The quantities of blood transfused following accidental losses are summarised in Table 5; most of the difference between oxymetholone and control periods is accounted for by 1 patient who was transfused for gastro-intestinal hæmorrhage.

TABLE II
Exclusions from the Trial

Started oxymetholone trial		55
Suitable for analysis		39
Excluded		16
Reasons for exclusion:		
Died		4
Received renal transplant		3
Transferred elsewhere		2
Pericardectomy		1
Did not send specimens regularly		1
Did not take tablets regularly:		
Intolerant to oxymetholone	2	
Intolerant to placebo	2	
"Tired of taking tablets"	1	
	—	5
		16

TABLE III
Periods of Treatment with Oxymetholone and Placebo

Oxymetholone 3 months, placebo 3 months	22
Oxymetholone 3 months, placebo 6 weeks	8
Oxymetholone 6 weeks, placebo 3 months	9
	39

TABLE IV
Changes in Hæmoglobin Concentration and Hæmatocrit

	Hæmoglobin (g./100 ml.)		Hæmatocrit (%)	
	Before	After	Before	After
Placebo	6·19	6·29	20·4	20·5
Oxymetholone	6·17	6·25	20·2	20·1

(3) *Effect on Liver Function Tests.*—SGOT levels were measured in 36 of the 39 patients completing the trial. One had elevated levels throughout, averaging 37 IU on placebo and 36 IU on oxymetholone. One patient had a single abnormal result on oxymetholone but subsequent results were normal although the drug was continued. Serum bilirubin and alkaline phosphatase

TABLE V

Blood Transfused to Replace Accidental Loss

	Total Units	ml./Patient/Month
During placebo	11	70
During oxymetholone	24	116

TABLE VI

Physical Signs Produced by Oxymetholone in 60 Patients

Severe pustular acne	1
Excessive seborrhœa	2
Facial hair growth	1
"Oxymetholone facies"	20

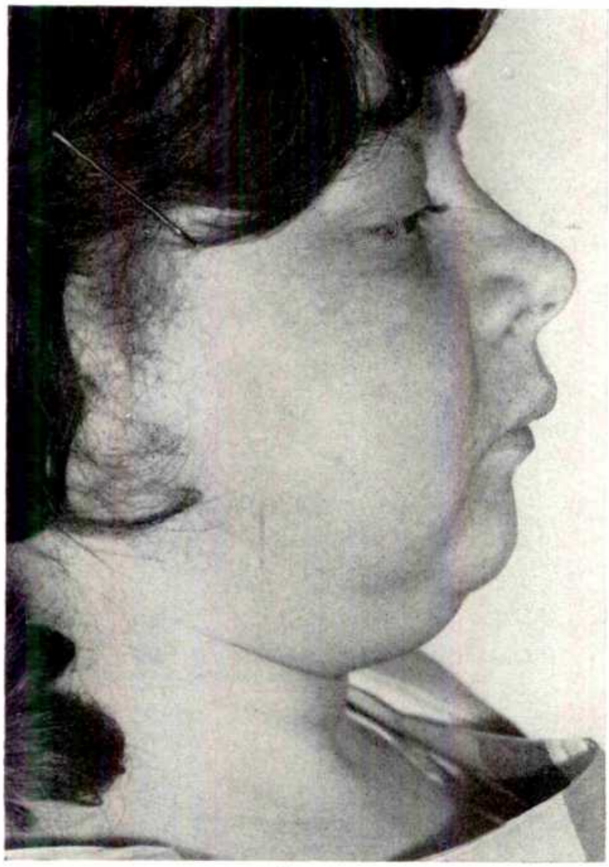


FIG. 1

Oxymetholone facies in a 23 year old woman; note the swollen cheeks and double chin which appeared during treatment with the drug and disappeared after its withdrawal.

levels were measured in 20 patients who completed the trial; bilirubin was normal throughout. Those patients with initially normal alkaline phosphatase remained normal and there were no significant elevations during therapy in those with raised serum alkaline phosphatase due to bone disease.

(4) *Other Side Effects.*—Thirty patients completed their symptom questionnaires conscientiously throughout. One woman noted facial hair growth and voice change while taking oxymetholone and her complaints were corroborated. Vomiting was mentioned 11 times in the oxymetholone period, 7 in the placebo. The only other complaints mentioned more than once were nausea, abdominal pain and heartburn, all equally distributed between treatment and placebo periods.

Table VI lists the physical signs observed in the whole group of 55 patients plus the 5 taking oxymetholone before dialysis. The " oxymetholone facies " (Fig. 1) is a characteristic combination of swollen cheeks, reminiscent of hamster pouches, a double chin, an overall rounding of the face and a thickened skin. The face had returned to normal within 6 months of stopping the drug except in 2 patients who still had traces of the changed configuration up to 1 year later.

We had hoped for a beneficial side effect of oxymetholone on the depressed sexual activity of our patients but the answers to the symptom questionnaire (Table VII) were not encouraging.

TABLE VII

Effect of Oxymetholone on Sexual Function in 30 Patients

		Placebo	Oxymetholone
Potency	depressed	5	6
	nil	9	8
Libido	depressed	7	8
	nil	9	8

Patients on Conservative Treatment.—Two patients required regular dialysis after 2 and 3 months of oxymetholone respectively. In both the hæmoglobin level fell steadily as uræmia advanced, in spite of oxymetholone. Two other patients abandoned treatment after 2 and 3 months because of alleged side effects—troublesome seborrhœa in one and loss of libido in the other. Both claimed improvement after stopping the drug; this was confirmed objectively in the case of the seborrhœa, Neither had any rise in Hb. The fifth patient took oxymetholone for 10 months. Apart from a pronounced oxymetholone facies he had no side effects. His Hb rose from 8·4 to 10·8 g./100 ml. Apart from a single SGOT level of 23 IU in the last patient, liver function tests were normal in this group.

DISCUSSION

Since this trial was conducted several authors have reported a hæmopoietic response to injected testosterone esters in patients treated by regular hæmodialysis (DeGowin *et al.*, 1970; Richardson and Weinstein, 1970; Shaldon *et al.*, 1970, 1971*a*, *b*). None of these studies was controlled and 2 were conducted on patients still receiving transfusions but their unanimity strongly suggests that testosterone is effective. The doses employed were 250 to 600 mg. weekly and at this very high level even the injected preparations of testosterone appear to carry a slight risk of producing jaundice (Richardson and Weinstein, 1970). Our reason for choosing an orally administered steroid was the fear of hæmatoma formation after large intramuscular injections in anticoagulated patients—1 of our dialysed patients sustained a sciatic palsy from a massive hæmatoma following a gamma-globulin injection. We also hoped that a less androgenic steroid would reduce the risk of masculinisation in women—particularly permanent voice change —and priapism in men (Shaldon *et al.*, 1971*a*).

We were successful in our negative aim of avoiding toxicity. Side effects were not distressing —though young women would not tolerate the oxymetholone facies indefinitely—and were reversible. At the dose of 100 mg. oxymetholone daily, which is much higher than that usually employed for anabolic action, we did not encounter liver toxicity. However, we would be hesitant to repeat the trial at a yet higher dosage since the use of oxymetholone in doses of several hundred mg. per day for hypoplastic anæmia has been attended by jaundice and deranged liver function tests in up to 80 per cent of patients (Sanchez-Medal *et al.*, 1969). Liver function usually returns to normal within a few weeks of withdrawing the drug but the administrative upheaval caused by any case of jaundice in a hepatitis-conscious dialysis unit is too great to justify the risk.

We demonstrated no benefit from oxymetholone in this safe dosage for 3 months. Response to oxymetholone and other androgenic drugs in hypoplastic anæmia is often delayed by a period of 2 weeks to 6 months (Sanchez-Medal *et al.*, 1969). However the great majority of those who are going to respond have started to do so within 3 months and the same applies to patients in renal failure receiving testosterone (DeGowin *et al.*, 1970; Richardson and Weinstein, 1970; Shaldon *et al.*, 1970, 1971*a*, *b*). We doubt therefore whether a longer trial of oxymetholone 100 mg. per day would have produced any better results.

We found only 5 patients on conservative therapy who merited trial of oxymetholone in a renal clinic which at any one time handles about 50 patients in various stages of chronic renal failure. This confirms our contention that anæmia in this group is not a major therapeutic challenge if one is concerned with treating symptoms, not laboratory results. McCredie (1969) treated 7 such patients with oxymetholone 100 mg. daily without success. Our only patient who responded had polycystic disease, a condition which is associated with persistent secretion of erythropoietin and the maintenance of a higher Hb throughout the course of renal failure than other renal diseases (Maggiore *et al.*, 1967). The 2 patients in our dialysis group who responded to vitamins and iron were also polycystics. Patients with this disease, who become anæmic from advanced uræmia or hæmaturia, merit treatment with hæmatinics and are probably more responsive to androgens than other uræmics since these drugs appear to act mainly by increasing secretion of erythropoietin (Gordon *et al.*, 1968; Rishpon-Meyerstein *et al.*, 1968; Alexanian, 1969; McCredie, 1969; DeGowin *et al.*, 1970; Shaldon, 1971*b*).

With the possible exception of patients with polycystic disease, oxymetholone in safe dosage has no role in the treatment of anæmia in renal failure. This leaves intramuscular testosterone as the only established drug therapy for the condition. The hazards or intramuscular injection are diminishing as the arteriovenous fistula displaces the arteriovenous shunt and the need for long-term anticoagulants disappears, but we view with alarm the prospect of indefinite treatment of female patients with high doses of this drug. There is an obvious need for more long-term studies of testosterone so that the side effects and considerable cost can be weighed against the benefits and further trials with less androgenic steroids should be pursued. Most orally effective agents share the disadvantages of oxymetholone but a few are not 17-alkylated and appear to carry a lower, though not negligible, risk of jaundice (Sanchez-Medal *et al.*, 1969). These, and the intramuscular drugs such as nandrolone decanoate, merit further study.

SUMMARY

Oxymetholone 100 mg. per day was given to 60 patients in chronic renal failure, 55 of whom were receiving regular hæmodialysis. Thirty-nine of the dialysed patients completed a cross-over double blind trial of oxymetholone, 30 of them taking the active drug for 3 months; there was

no significant change in hæmoglobin or hæmatocrit. No significant change occurred in liver function tests and the only side effect that appeared more than occasionally was a characteristic fattening of facial tissues which reverted to normal after withdrawal of the drug.

One patient with polycystic disease treated by Giovannetti diet sustained a rise in hæmoglobin from 8·4 to 10·8 g./100 ml. while taking oxymetholone for 10 months.

On present evidence oxymetholone in safe dosage has little or no role in treating the anæmia or renal failure, but trials of other anabolic steroids with less masculinising effect than testosterone should continue.

We would like to thank the nursing staff of the dialysis units, particularly Sister S. Tulip, and Mrs K. Holmes, formerly Dialysis Administrator, for their help in the administration of the trial. Syntex Pharmaceuticals Ltd. for supplies of oxymetholone and placebo and Dr Miriam Moore-Robinson for advice and assistance.

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ARTERIO-VENOUS SHUNTING OCCURRING WITH REJECTION IN A RENAL TRANSPLANT

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RENAL angiography may be used in the diagnosis of rejection of transplanted human kidneys. The angiographic signs of rejection, previously reported, have been: (1) swelling of the kidney with tapering interlobular arteries of unequal calibre, (ii) slowing of the transit time of contrast medium through the renal vasculature and (iii) blockage of interlobular arteries.

This report describes diffuse arteriovenous shunting of contrast medium within a rejected renal graft.

Case Report.—A 45-year-old woman, who had been having hæmodialysis treatment for 6 months (because of renal failure secondary to pyelonephritis and hypertension), had a cadaver kidney transplant in January 1970. Tissue typing showed donor/recipient compatibility and a cross-match between the donor's red blood cells and the recipient's serum was negative. Silver clips were placed on both poles and the lateral border of the grafted kidney for measuring its size, using plain abdominal radiographs in the manner described by Fletcher and Lecky (1969). Following transplantation she had five hæmodialysis treatments. Diuresis was well established by the 12th post-operative day, and the creatinine clearance was 30 ml. per minute on day 16.

The first episode of rejection occurred on the 19th day, and a 5 per cent. increase in graft length (from 14·0 to 14·7 cm.) was demonstrated on the plain radiographs. Following increased doses of steroids (prednisolone) the graft became smaller (14·1 cm.) and the creatinine clearance increased to 40 ml./minute. The second episode of rejection started on the 39th day and continued despite high doses of steroids, actinomycin-c, azathioprine and 2 doses of radiotherapy (totalling 300 rads.). Hypertension with diastolic pressures varying between 100 and 300 mm./Hg was present throughout the post-operative period, and was treated with methyldopa. Her own diseased kidneys were not removed. The graft was biopsied on the 47th day, the biopsy showing thickening of the glomerular basement membranes and the mesothelia of the blood vessels, intimal fibrosis and necrosis of arteries, aproximal tubular necrosis (some tubules being filled with eosinophilic material) and interstitial œdema (with infiltration by lymphocytes and plasma cells, areas of hæmorrhage and fibrosis). These findings were interpreted as showing severe rejection.

We carried out an angiogram on the 48th post-operative day, by which day the creatinine clearance had dropped to 2 ml./minute. The tip of the catheter was placed in the left common iliac artery and 20 ml. diatrizoate (Urografin 60 per cent.) was injected rapidly by hand. The angiogram showed cortico-medullary shunting of contrast medium with opacification of the renal and iliac veins within 2 seconds, which we considered diagnostic of rejection (Figs. 1, 2 and 3).

Hæmodialysis was recommenced on day 51, and the graft was removed 4 days later. At operation the graft was black in colour and congested. It weighed 220 gm. The major vessels and the ureter were patent. Histological examination showed that there was severe intimal fibrosis of the small intra-renal arteries and afferent glomerular arterioles with areas of marked fibrinoid necrosis. In addition there were glomerular capillary thromboses and basement membrane thickening. Tubular damage was extensive with areas of tubular necrosis and degenerating epithelium. As in the biopsy specimen many tubules were filled with eosinophilic material. The interstitial tissues showed hæmorrhage and fibrin deposition, but there was little cellular infiltration.

DISCUSSION

The first reports of the use of arteriography in the diagnosis of rejection of transplanted kidneys were made by Alfridi, Meany, Boncove and Nakamoto (1966), O'Connor, Dealy, Lindquist and Couch (1967) and Staple and Chiang (1967). Non-rejecting renal transplants usually show well-defined cortical arteries with only slight tortuosity, and a normal differentiation of the cortex from the medulla in the nephrographic phase. In kidneys undergoing rejection the contrast medium may clear more slowly from the arteries (than in those which are not being rejected), and the flow rate may be compared with that in neighbouring tissues such as the back

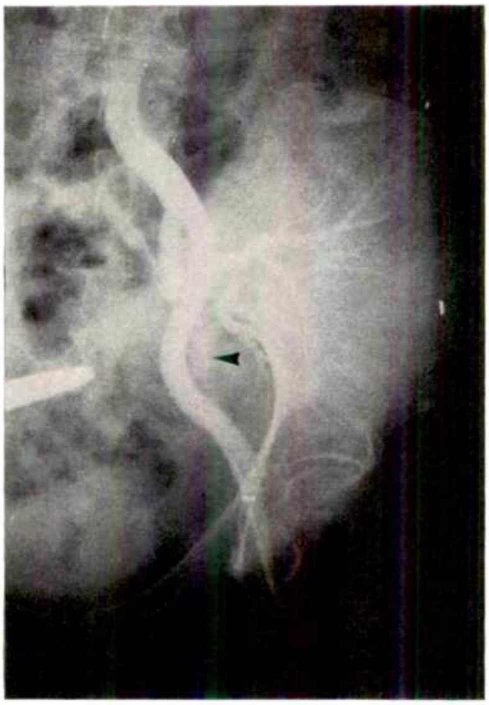

FIG. 1

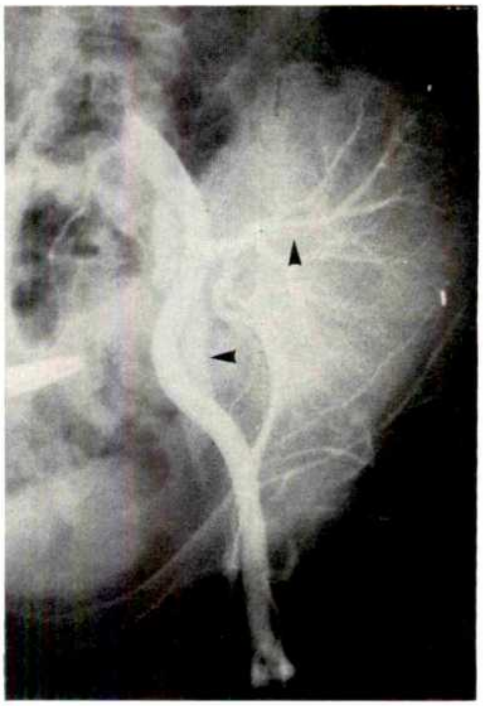

FIG. 2

Fig. 1.—Angiogram of the renal transplant, the radiographic exposure being made before the injection had been completed. Note that the renal and iliac (arrowed) veins had already been opacified.

Fig. 2.—Two seconds later, the left iliac vein is well opacified and the tributaries of the renal vein are well seen.

Fig. 3.—After a further 2 seconds the pelvic veins and the inferior vena cava (arrowed) are demonstrated whilst the arteries have largely cleared. (Note: residual contrast medium remains in the bladder from a cystogram carried out to exclude reflux the preceding day).

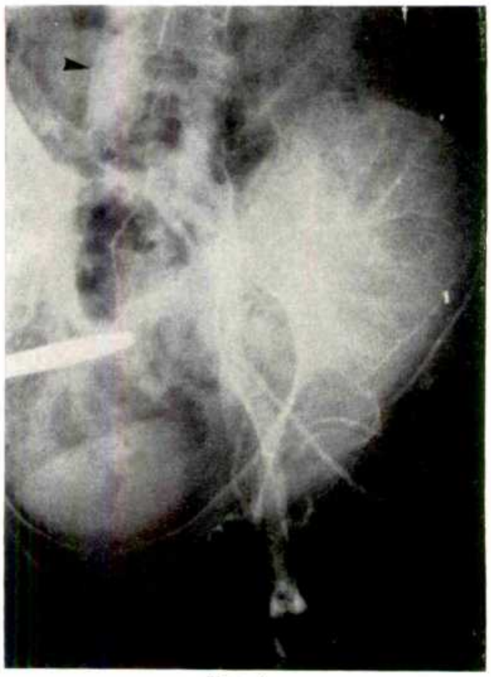

FIG. 3

or the buttock. Nilson *et al.* (1969) and Rosenberger *et al.* (1970) pointed out that if the contrast medium takes more than 3 seconds to clear from the renal arteries, following a common iliac artery injection, rejection is very likely. Vinik *et al.* (1969*a*) similarly showed that rejection is likely when the injection is made selectively into the main transplant artery and the contrast medium remains in it for more than 1·25 seconds after the end of the injection.

Œdema, of the kidney being rejected, causes it to swell with elongation, tapering, splaying and irregular calibre of the interlobular arteries. In chronic rejection interstitial fibrosis causes " crowding " of these vessels. The nephrogram in rejection varies from normal to absent; Raphael *et al.* (1969) considering that the variability had no prognostic significance. On the other hand Samuel (1970) showed that the nephrogram may demonstrate swelling of the renal pyramids before any arterial changes may be present.

In our patient the arterial blood flow into the kidney was fast, and before the injection of the contrast medium was finished some had already reached the renal vein through its tributaries (Fig. 1). Two seconds after the start of the injection, contrast medium had reached the iliac veins (Fig. 2), and it could be seen in the inferior vena cava after a further 2 seconds (Fig. 3).

Vinik *et al.* (1969*b*), studying renal grafts in dogs, showed that contrast medium normally appeared in the renal veins 2 to 8 seconds after the end of the injection. In 14 out of 17 rejecting kidneys, contrast medium either did not appear in the renal veins at all, or it appeared more than 8 seconds later. In the other 3 kidneys very rapid arterio-venous shunting of contrast medium occurred similar to that seen in our patient.

The first demonstration of arterio-venous shunting in the kidneys was made by Trueta *et al.* in 1947, and it has since been termed the "Oxford Phenomenon " or "Trueta Phenomenon ". They found a blanching of the renal cortex in the kidneys of rabbits and rats in response to electrical stimulation of sciatic or splanchnic nerves, rapid severe hæmorrhage or the intravenous injection of staphylococcal toxin. It was postulated that this shunting was the basis of the war-time " crush syndrome ", in which renal impairment leading to death occurred following the release of compression of a trapped limb. Similar renal failure, " traumatic uræmia ", was also seen following severe hæmorrhage (Darmady, 1947). Edsman (1957), and Siegelman and Goldman (1968) demonstrated the phenomenon angiographically in human kidneys (not transplanted) and thought that the cortico-medullary shunt could be due to a variety of causes including hypotensive shock. In transplanted kidneys in dogs Almgard *et al.* (1966) have shown arterio-venous communications in the periphery of the cortex due to rupture of the vessel walls during rejection. Rosen *et al.* (1967) using a radio-active xenon wash-out technique showed that as rejection of canine renal transplants progressed the area of cortex perfused was progressively reduced until the fastest flowing component was located in the outer medulla. Renal vascular shunts of differing types have also been discussed by Elkin (1971), who was uncertain about the true physiological nature of the " Oxford shunt ".

We believe that arterio-venous shunting in a human renal transplant may be a further sign of rejection, and in our patient the rejection was so far advanced that the kidney had to be removed.

SUMMARY

Angiography of a human transplanted kidney showed arterio-venous shunting (the " Oxford or Trueta phenomenon "). The presence of this phenomenon in a renal graft may be a further sign suggesting rejection.

We wish to thank Dr J. G. G. Ledingham for his advice, and Dr M. S. Dunnill for the pathological findings. The prints were prepared by the Department of Medical Illustration, United Oxford Hospitals.

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SEGMENTAL ACUTE PYELONEPHRITIS

A Precursor to Renal Carbuncle or Abscess?

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PYELONEPHRITIS is generally accepted as a disease which involves both kidneys diffusely unless there is a predisposing factor on one side only. The purpose of this paper is to report 2 cases of acute pyelonephritis which appeared to involve only a segment of 1 kidney. The clinical significance of this finding, its existence as a pathological entity and its possible relationship to intra-renal suppuration will be discussed.

Case 1.—Mr G., aged 34, had been well until 2 days prior to admission, when he developed bilateral renal angle pain, and pain in the right iliac fossa. The next day he noticed some difficulty and burning on micturition.

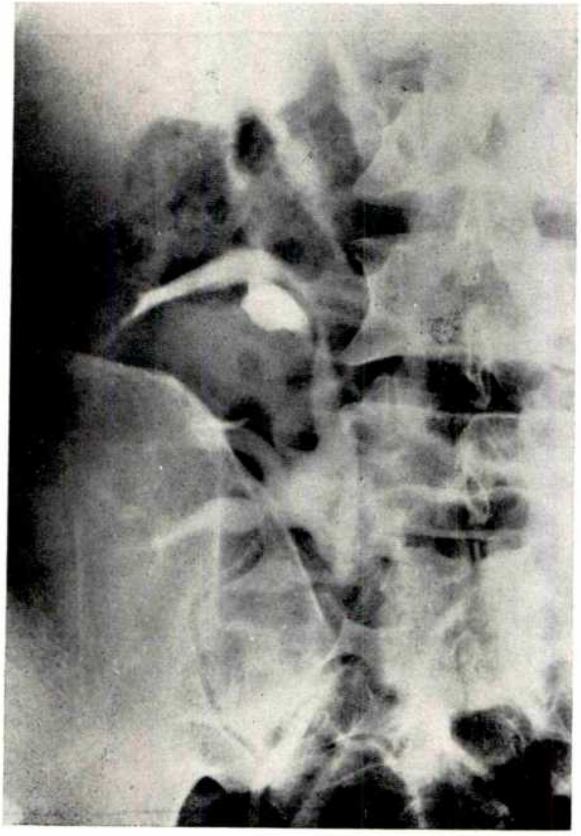


FIG. 1

Case 1. Intravenous pyelogram showing a bifid collecting system apparently stretched out over an intrarenal mass.

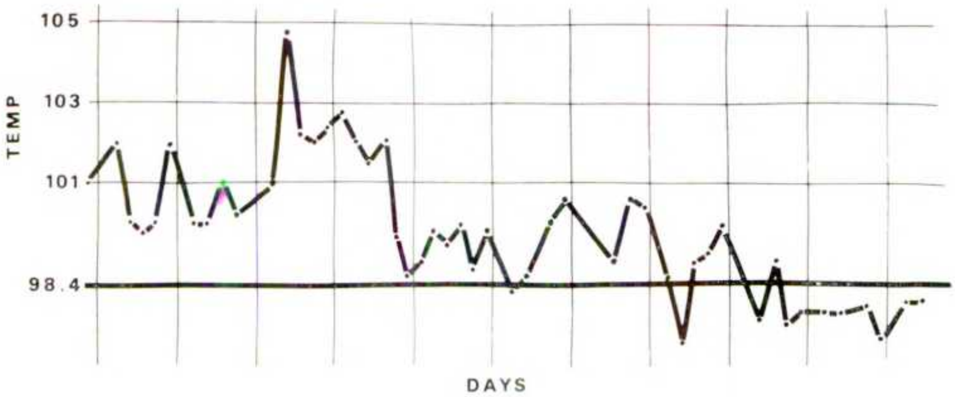
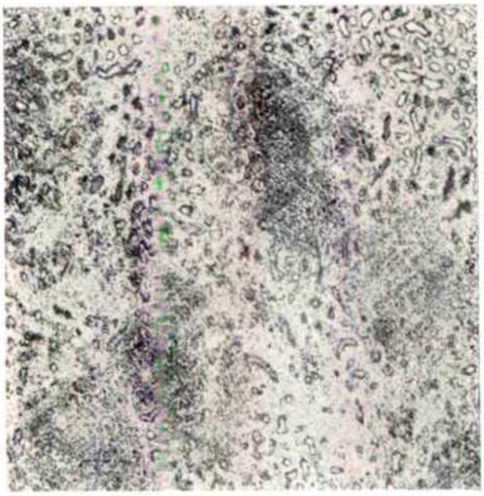


FIG. 2

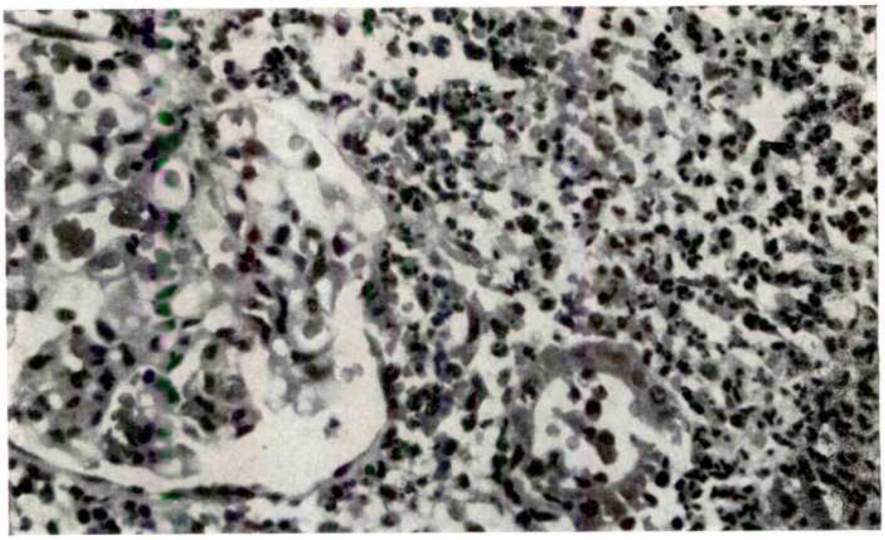
Case 1. Temperature chart illustrating the clinical course.



A

FIG. 3

A, Histology showing micro-abscesses in renal cortex. (Case 1. H. & E. ×15). B, Histology showing purulent infiltrate around a glomerulus. (Case 1. H. & E. ×240).



B

In addition he had vomited 4 times. On examination he was ill with a temperature of 102°F. His pulse was 90 per minute and blood pressure was normal. Abdominal examination revealed a tender mass in the right iliac fossa which extended up towards the right loin. The mass was mobile but guarding and rebound tenderness was present over it. On rectal examination there was tenderness and possibly some bogginess in the rectovesical pouch. Microscopic examination of the urine showed numerous white blood cells, and on culture grew E. coli, the colony count being between 10,000 and 100,000 organisms per ml. His white cell count was 12,800 per cu. mm. and his blood urea was normal. An intravenous pyelogram showed a bifid pelvis and collecting system which appeared to be stretched out over a central intra-renal mass (Fig. 1). In view of the patient's severe illness he was immediately started on a course of Gentamicin, 60 milligrams 8-hourly intramuscularly. Urine cultured the next day and on subsequent occasions was sterile. The patient's clinical course is well illustrated by his temperature chart (Fig. 2). After 48 hours treatment, without any clinical response and persistence of severe pain, exploration of this intra-renal mass was decided upon. In view of the possibility of an underlying renal cyst, tuberculoma or necrotic carcinoma, an arteriogram was performed. This showed two renal arteries, one arising from the aorta and the other from the common iliac artery. It did not, however, demonstrate displacement of vessels or new vessel formation to indicate the nature of the renal mass. At operation through a right iliac fossa extraperitoneal approach, the perirenal fascia was opened revealing scanty, slightly œdematous perinephric fat. A swab taken from this tissue for culture was sterile. The kidney was mobilised easily. Its central area was occupied by a swelling with the consistency of normal renal tissue. Attempted aspiration of this area was unproductive. On stripping the capsule the affected area appeared darker than normal, and the surface was studded with numerous pinhead size abscesses. A large biopsy was taken. No pus was encountered and the renal tissue bled poorly. Culture of this tissue grew E. coli. The histological report was that of an acute pyelonephritis with numerous micro-abscesses (Fig. 3). Post-operatively the patient's pain was immediately relieved. Twelve hours later he was still severely toxæmic with a temperature above the pre-operative level. Cephaloridine, 500 milligrams 8-hourly had been added to his treatment immediately prior to operation. From the second post-operative day the patient's condition improved and settled completely. An intravenous pyelogram done 2½ months post-operatively showed a persistence of the calyceal deformity, but the displacement appeared to have decreased.

Case 2.—Miss J. v. V, aged 8, was admitted to the care of the pædiatricians with a history that for the previous 2 months she had been enuretic with increased frequency of micturition of large volumes of urine, associated with burning on micturition. She had been treated as an outpatient with a sulphonamide at an outlying hospital. Two days prior to admission she complained of headache, abdominal and chest pain, and a sore throat. The pain was most marked in the right hypochondrium and was aggravated by movement. On examination she was ill and flushed. Her pulse rate was 140 per minute and blood pressure was 118/80 mm. Hg. Abdominal examination showed some tenderness of the whole of the left side and in the right lumbar region. She was investigated as a pyrexia of unknown origin. Urine examination revealed no abnormality. Her clinical course is well illustrated by her temperature chart (Fig. 4). When seen in consultation on the sixth and seventh days following admission, the child appeared to have recovered completely. Her voiding cysto-urethrogram showed a small amount of dye in the middle and upper calyces of the right kidney. The intravenous pyelogram showed medial displacement of the upper and lower calyces, and apparent compression of the middle calyx. A bulge was just detectable on the lateral border of the kidney (Fig. 5). In view of the absence of symptoms or signs it was decided to keep her under observation. On the ninth day she became pyrexial and toxæmic with rigors, but no localising physical signs were detected on examination. The intravenous pyelogram was repeated but showed no change, and the kidney moved freely with respiration. A diagnosis of intra-renal abscess was made. Gentamicin and Sodium Cephalothin were administered intramuscularly and 5 hours later the kidney was explored surgically. On opening the perirenal fascia the kidney was found to be freely mobile. A swelling consistent with the X-ray finding was present in the mid-zone, the area appearing normal through the kidney capsule. The upper pole however, appeared blue. Attempted aspiration of these areas was unproductive. On splitting the kidney capsule, the central area was dusky red, while the upper pole was deep blue. The whole area was studded with pinhead size

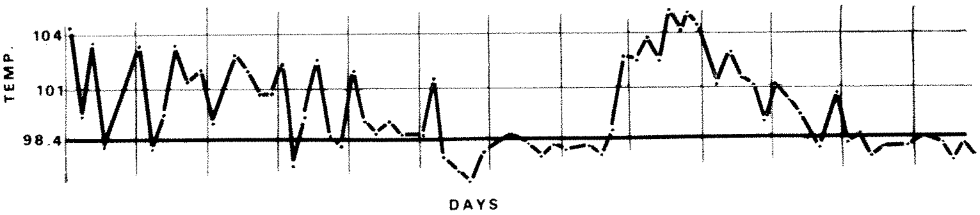


FIG. 4
Case 2. Temperature chart illustrating the clinical course.

micro-abscesses. Biopsies taken from the central area bled reasonably freely, while those taken from the upper pole did not bleed at all. A drain was inserted. The patient's post-operative course was uncomplicated. Culture of the kidney substance revealed Enterobacter cloacæ. The histology showed even more severe acute pyelonephritis with micro-abscess formation than in case 1. Blood cultures which had been sent pre-operatively were sterile.

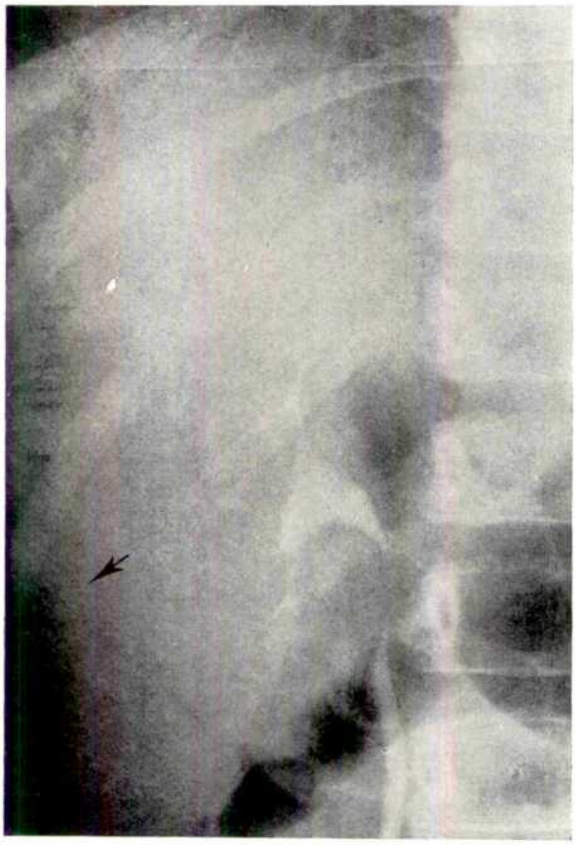


FIG. 5

Case 2. Intravenous pyelogram showing medial displacement of the upper and lower calyces and apparent compression of the middle calyx. A bulge (arrowed) is just detectable on the lateral border of the kidney.

DISCUSSION

Heptinstall (1966) has pointed out that the macroscopic and microscopic pathology of the usual clinical form of acute pyelonephritis is not known, as these patients are not usually submitted to renal biopsy. The available pathological descriptions of acute pyelonephritis are derived from cases of infection as seen at autopsy when both kidneys are diffusely involved. The pathological features seen in the affected area in the cases described above fit this description, except that macroscopically the lesion appeared to be localised to a segment of the kidney.

A renal abscess or carbuncle is an uncommon form of renal infection, which affects a segment of the renal parenchyma (Graves and Parkins, 1926; Cobb, 1966). The clinical diagnosis is difficult, and usually surgical exploration is only undertaken when spread has occurred into the perinephric tissues with the formation of a perinephric abscess. Primary intra-renal abscesses are invariably due to hæmatogenous spread of Staphylococcus aureus from some other lesion, most commonly in the skin, which has frequently healed and been forgotten at the time of presentation of the renal lesion. In the past acute hæmatogenous staphylococcal pyelonephritis was considered to be a fairly common condition which seldom progressed to the complication of intra-renal suppuration (Nesbit, 1940). Today it is considered to be an uncommon illness (Harrison, 1970). Renal abscesses due to gram-negative bacteria have been reported from time to time, but these are usually associated with previous renal disease. A case of renal abscess due to E. coli infection in an otherwise normal kidney has been reported (Fair and Higgins, 1970).

Once an abscess is present surgical principles dictate that drainage is essential. However, it has been claimed that there are 4 cases of renal carbuncle in the literature which have responded to conservative therapy (Cobb, 1966). The clinical picture in these cases is so similar to that of the 2 cases reported above that it suggests that they may also have been cases of an essentially localised severe acute pyelonephritis. These cases, too, demonstrate that at this stage of the disease it is impossible to differentiate between the phase of pyelonephritis and of abscess formation.

Doolittle and Taylor (1963) pointed out the difficulties in diagnosis of a renal abscess and that a correct pre-operative diagnosis was made in only one-sixth of the reported cases. The accumulating experience in the literature, the clinical picture of a pyrexial illness, together with the radiological sign of a space-occupying lesion in the kidney should make a pre-operative diagnosis possible in a greater percentage of cases. Renal arteriography could be of value in arriving at a diagnosis. However, instances have been reported in which inflammatory lesions have shown new vessel formation, suggestive of a renal carcinoma (Land and Rosen, 1970). In these cases the malignant-like characteristics were not very marked.

On the evidence presented the cases we have reported seem to represent examples of pyelonephritis, which appear to be unilateral and macroscopically affect a segment of a kidney only. The question also arises as to whether these cases are truly examples of primary pyelonephritis. Dysplasia may be an ætiological factor in case 1, whilst in case 2 reflux may be implicated as a predisposing factor. The reflux may, however, equally well be a result of the renal infection.

These cases suggest that bacterial infection of the renal parenchyma should be looked upon as a spectrum of disease entities:

1. Acute pyelonephritis in its usual clinical form, the histological picture of which is uncertain.
2. Severe acute pyelonephritis with micro-abscess formation, as seen occasionally at post-mortem examination (Heptinstall, 1966).
3. An apparent rare localised form of acute pyelonephritis which may present as a severe and serious illness, and may mimic a renal abscess or carbuncle. Two examples of this condition are presented in this paper. The cause of this lesion is not always evident, but it may be reasonable to deduce that an area in a kidney affected by acute pyelonephritis may show progression of the pathological process, while the rest of the organ undergoes healing; or that the infection may have been segmental from the beginning as a result of hæmatogenous spread, due to bacteræmia or septic embolisation, as is acceptable in the pathogenesis of renal abscess and carbuncle. This stage of renal infection may heal or progress to 1 of the next 2 stages. It also follows that a renal carbuncle or abscess must have developed through the stages mentioned above. During this phase of the disease clinical diagnosis may not be possible because there may not be any deformity visible on pyelographic examination. This situation was present in the upper pole of the kidney in case 2.
4. A renal carbuncle should only be diagnosed when a circumscribed area containing multiple macroscopic abscesses, which may communicate with each other, can be found in the renal substance. This is comparable with the carbuncle of the subcutaneous tissue which consists of a series of communicating abscesses which discharge through separate openings on to the surface;

the condition is associated with a marked fibroblastic reaction. These abscesses may be small and associated with so much fibrosis that drainage is not possible and excision is then required.

5. A renal abscess which consists of a single abscess cavity in the renal substance.

TREATMENT

The treatment of this spectrum of disease entities is well established at its extremes, being conservative at the one end and involving surgical drainage at the other; the latter, in practice, usually consists of drainage of a perinephric abscess. There is, however, a group of patients who present the clinician with a problem as to which group they fall into, and therefore which form of treatment is indicated. The cases reported above appear to present a further diagnostic problem of a similar nature, namely—is pus present in the renal parenchyma, or not? As the clinical presentation is usually one of a severe infection, possibly with septicæmia, a period of conservative therapy would appear to be indicated (McAllister, 1945). An area of acute segmental pyelonephritis may then subside completely. In this context it is possible that case 2 above may have been explored too early. In case 1 there was no response to conservative therapy and therefore exploration was justified. Splitting the renal capsule and relieving the intra-renal tension appears to have had some beneficial effect. On the first post-operative day the temperature rose alarmingly and it appeared at the time as though nephrectomy may have been the wiser course.

SUMMARY

Two cases of apparently segmental pyelonephritis encountered at surgical exploration of the kidney are presented. It is postulated that this is a stage in the spectrum of acute inflammatory lesions of the kidney which falls between acute pyelonephritis on the one hand and renal abscess or carbuncle on the other. In clinical practice the diagnosis is infrequently made at this stage because the radiographic appearances indicative of a localised space-occupying lesion are not necessarily present. Antibiotic treatment during this stage of the disease may be adequate. However, because of the difficulty in deciding whether an abscess is present or not, failure of the clinical and radiological response to treatment would indicate the necessity for surgical exploration.

We thank the Superintendent of the Johannesburg General Hospital for permission to report these cases, and the Director of the South African Institute for Medical Research for granting us facilities. Our secretaries and the photographic departments gave us invaluable help for which we are grateful.

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HORMONAL INFLUENCE ON THE ADRENERGIC RECEPTORS OF THE URETER[1]

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The well-recognised fact that dilatation of the ureters occurs in a large proportion of pregnancies has resulted in much discussion as to whether the cause is mechanical, due to pressure on the ureters by the enlarging uterus, or hormonal in response to the changes in the level of circulating hormones during pregnancy. Whatever part mechanical pressure may play, there is by now well-documented evidence that changes in the female hormone milieu affect the ureter. Hundley and Diehl (1945), by direct measurement in women, demonstrated a pronounced increase in peristaltic activity of the ureter on giving œstrogenic substances, and a diminution, reaching atonia, following progesterone. Perhaps the most convincing experiments were those of Van Wagenen and Jenkins (1939), who demonstrated the development and maintenance of hydro-ureters in pregnant Rhesus monkeys after removal of the fœtus, where the hormonal effect was maintained by persistence of the maternal surface of the placenta. More recently, a number of reports have appeared of ureteric dilatation in women taking oral contraceptives (Marshall *et al.*, 1966; Guyer and Delany, 1970). In view of the evidence that a hormonal effect on the ureter does indeed exist, it is of interest to consider its possible mode of action.

As long ago as 1906, both Cushny and Dale drew attention to a change in the reaction of the pregnant as opposed to the virgin cat uterus, in response to hypogastric nerve stimulation or the intravenous injection of adrenalin. This " pregnancy reversal ", as Dale termed it, has subsequently been shown to be due to a change in the relative dominance of one or other of the adrenergic receptors.

The presence of both α and β adrenergic receptors in the ureter has been demonstrated, both by Trendelenberg's technique (Dean, 1967) and by the isometric method (Malin *et al.*, 1968), and it was, therefore, decided to investigate whether or not changes in the female hormonal milieu might produce a comparable " reversal " of adrenergic response in the ureter also, and hence, perhaps, indicate a possible mode of action of the hormones on the ureter during pregnancy.

Materials and Methods.—Thirty mature uncastrated female albino rats (Lewis strain) weighing 200-250 g. each were divided into 7 groups, and were given daily intraperitoneal injections according to the following protocol:—

Group 1—Control-physiological saline 1 cc.	(6 rats)
Group 2—Oestradiol Diproprionate 0·2 mg./k.	(4 rats)
Group 3—Progesterone 5 mg./k.	(4 rats)
Group 4—Oestradiol Diproprionate 0·2 mg./k.+Progesterone 5 mg./k.	(4 rats)
Group 5—Propranolol (Inderal) 3 mg./k.	(4 rats)
Group 6—Progesterone+Propranolol (in the above doses)	(4 rats)
Group 7—Progesterone+Propranolol+Oestradiol Diproprionate (in the above doses)	(4 rats)

After a period of treatment of from 5 to 21 days the ureters were exposed through a mid-line incision under ether anæsthesia, carefully dissected free to avoid stretching, and segments of

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[1] This investigation was carried out in the Surgical Research Laboratories of the Hebrew University-Hadassah Medical School, and supported by a grant from the Joint Research Fund of the Hebrew University and Hadassah Organisation, Jerusalem, Israel.

1·5 to 2 cm. long removed from the mid-portions. These were immediately placed in Locke's solution No. 2 at 5°C. The response of each ureteric segment was then studied by the isometric technique in a 50 cc. muscle chamber containing Locke's solution No. 2 at 38°C, ærated by 97 per cent O_2 with 3 per cent CO_2. The muscle tension was measured by a Grass force displacement transducer (FTO 3C), and recorded on a Sanborn recorder. A sensitivity of 25 mm. pen deflection per gram tension was used, and the paper recording speed was 0·25 mm./second. The ureters were subjected to a tension of 1 g., and the appearance of spontaneous activity described by Malin *et al.* awaited. Those ureters which did not recover spontaneous activity after one hour were excluded from further study. In those in which spontaneous activity did return, the reaction to the addition of 10 γ/ml. of adrenaline to the fluid in the muscle chamber was tested.

Results.—In the control group 9 out of the 12 ureters regained spontaneous activity, usually in about 25 minutes. This spontaneous activity was characterised by regular rhythmic contractions at the rate of 4-5 per minute. The addition of the adrenaline to the control group resulted in a slowing of the frequency of contractions to about 2-3 per minute (Fig. 1).

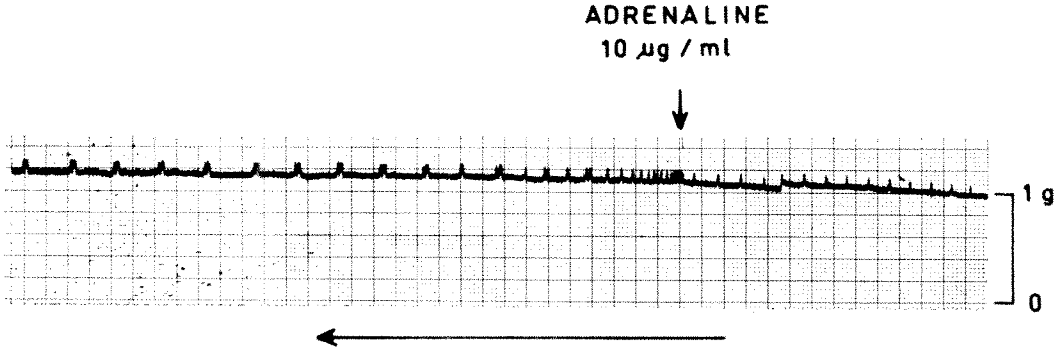

FIG. 1
Ureteric activity in control group. Addition of adrenaline reduces frequency of contractions.

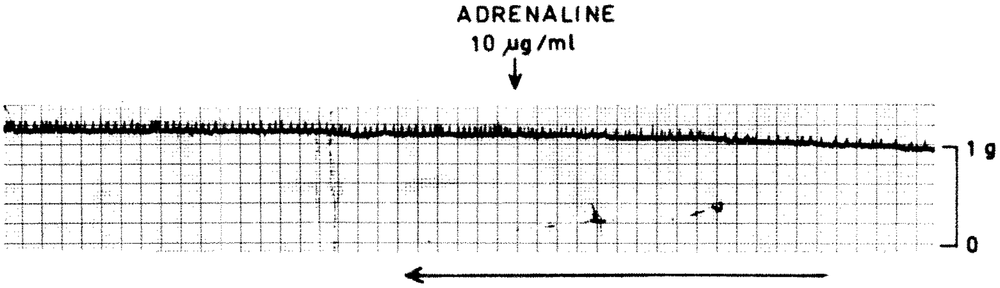

FIG. 2
Oestrogen-treated group. Spontaneous activity increased. Further increase on addition of adrenaline.

In the second group, those pre-treated with œstradiol, spontaneous activity appeared in 6 out of 8 ureters. In these the rate of spontaneous contraction was greater than in the control group (6-7 per minute), and the addition of adrenaline, instead of reducing the frequency as in the control group, now had a pronounced stimulating effect, increasing the frequency to 10 or more contractions per minute (Fig. 2).

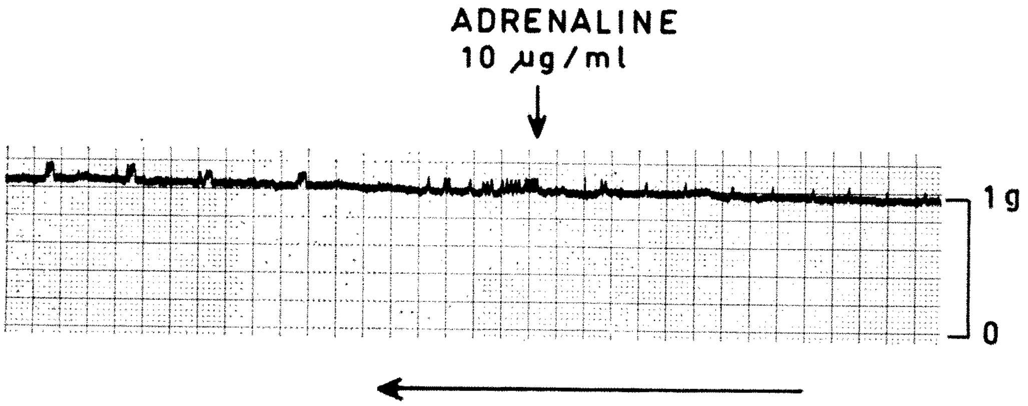

FIG. 3
Progesterone-treated group. Spontaneous activity less than in control group. Further reduction on addition of adrenaline.

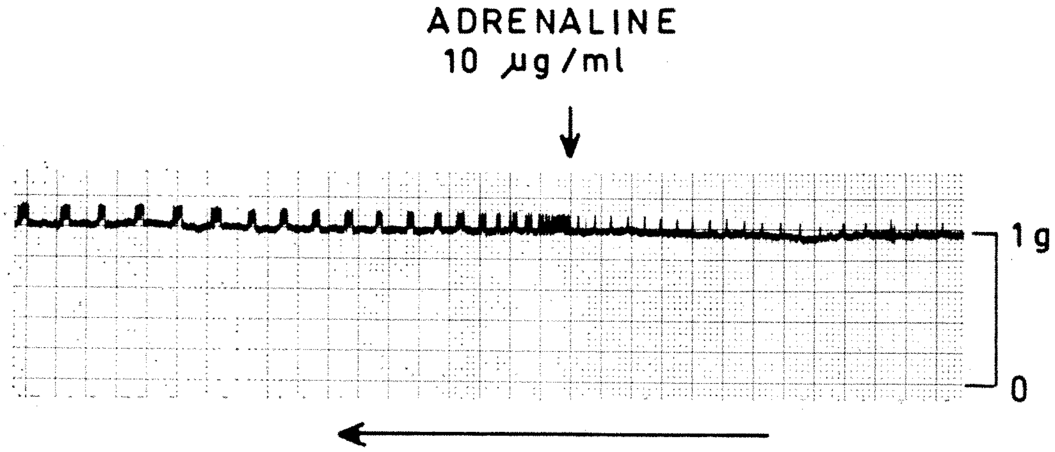

FIG. 4
Combined œstrogen-progesterone treatment. Reduced activity on adrenaline addition.

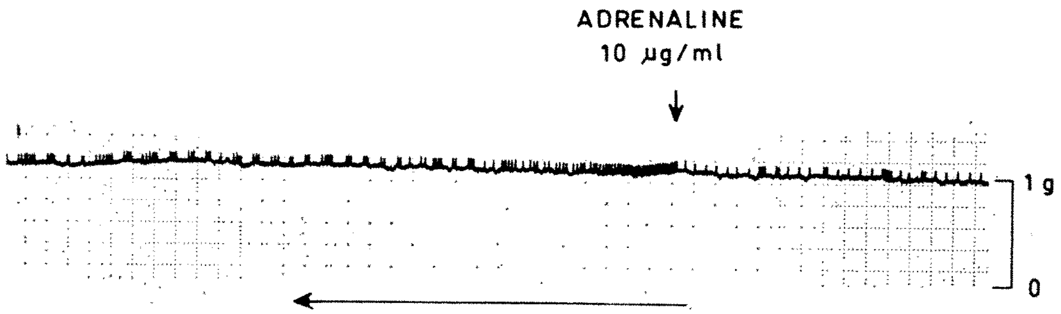

FIG. 5
Pre-treatment with Inderal blocks β-receptors. Increased spontaneous activity and further increase in response to adrenaline.

In group 3, those pre-treated with progesterone, only 4 out of 8 ureters recovered spontaneous activity, and when it appeared the contractions were much less frequent than in the control group (approx. 2 per minute). The addition of adrenaline in this group produced further slowing of the contraction rate (Fig. 3).

In the animals pre-treated with both œstradiol and progesterone (group 4), spontaneous activity was less than in the control group, but slightly more than in group 3. Here again, addition of adrenaline caused slowing of the contraction rate (Fig. 4).

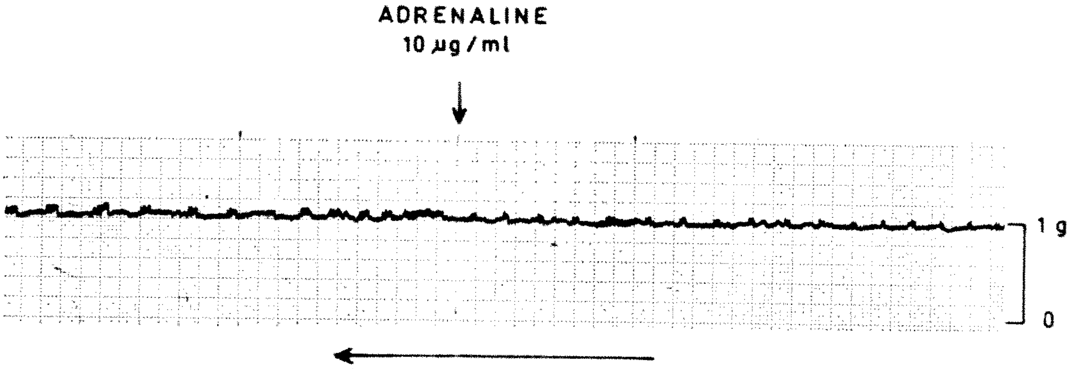

FIG. 6
Combined Inderal and progesterone treatment reduces spontaneous activity. Adrenaline produces further slowing.

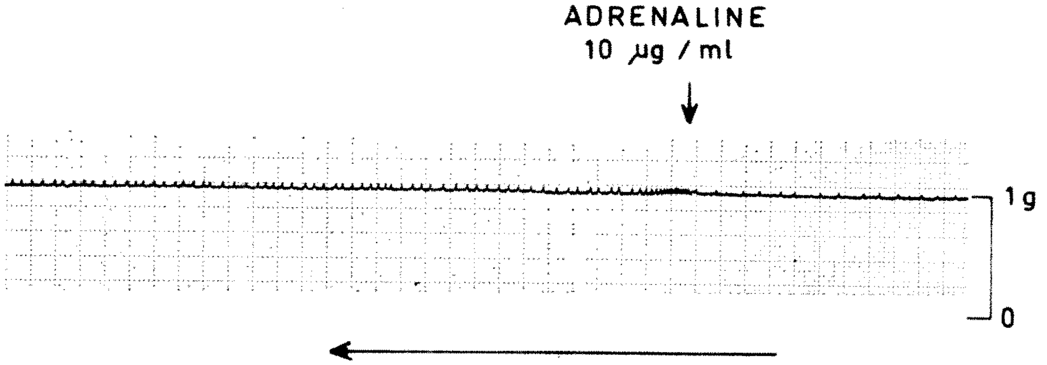

FIG. 7
Pre-treatment with Inderal + progesterone + œstrogen. Spontaneous activity similar to controls. Adrenaline produces increased activity.

In group 5, following treatment with the β-adrenergic blocker Inderal, spontaneous activity was more frequent than in the control group, and the reaction to adrenaline now consisted of a marked increase in the contraction frequency (Fig. 5).

When the pre-treatment consisted of both Inderal and progesterone (group 6), the spontaneous contraction rate was slower than in the control group or than in group 5 (slightly more than 2 per minute), and the adrenaline response consisted of further slowing (Fig. 6).

Those pre-treated with all 3 drugs (group 7) showed spontaneous activity similar to the control group, but a reversal of the adrenaline effect, which now produced an increased frequency of about 7-8 per minute (Fig. 7).

DISCUSSION

Malin and his colleagues (1970) have demonstrated the presence of both α- and β-adrenergic receptors in the ureter, α-receptor stimulation resulting in increased frequency and amplitude of contraction, and stimulation of the β-receptors having the opposite effect. Adrenaline contains both α- and β-stimulators, and thus its resultant effect upon organs with both types of receptors depends on the net effective preponderance of a given receptor.

In the present study it is seen that the net response to adrenaline in the control group (group 1) was a diminution of the frequency of contractions, *i.e.* a β-effect. Owing to the delicacy of the rat ureter, variations in the force of contraction or in the resting tone are minimal, and cannot be used as an index in this study.

In the group pre-treated with œstradiol (group 2) there is evidence of increased α-effect in the spontaneous activity of the ureters, and the addition of adrenaline now produces an α-effect with increased frequency of contractions, instead of the β-effect seen in the control group. Those animals pre-treated with progesterone, on the other hand (group 3), evidenced signs of β-overactivity, with reduction of the spontaneous activity, and a further depression on adding adrenaline. This effect was sufficient to outweigh the effect of the œstradiol, in the doses used, when both drugs were used together, as exemplified in group 4.

As would be expected, pre-treatment with Inderal, an effective β-blocker, left the α-receptors in a relative preponderance (group 5), so that spontaneous activity in this group was slightly greater than in the control group, and the effect of the addition of adrenaline was now clearly α-in nature—the β-effect seen in the control cases having been suppressed. However, when the pre-treatment with Inderal was combined with progesterone (group 6), it is evident that, in the doses used, the Inderal was no longer able to block the β-receptors effectively, and the net result both in the resting ureter and in response to adrenaline was a β-type response. The combined effect of the œstradiol (enhancing the α-effect) plus the Inderal (blocking the β-effect) was, however, sufficient to outweigh the β-enhancing effect of the progesterone (group 7), and the net response to adrenaline in this case was α-in nature.

The results of these experiments may be summarised by stating that, in the rat ureter, pre-treatment with progesterone produces an increase in the β-adrenergic response, whilst pre-treatment with œstradiol produces a similar effect upon the α-receptors.

The exact mechanism of the effect of the female hormones on the adrenergic reaction of the ureter is not clear. In the case of the uterus, which may in some degree be comparable as having a similar embryological origin, similar effects have been described by a number of workers (Miller and Marshall, 1965; Diamond and Brody, 1966; Wansbrough *et al.*, 1968). Sjöberg (1968) produced histochemical evidence of a marked increase of noradrenaline in the uterus and vagina in animals treated with œastrogen, and Falck and his co-workers (1969) showed that this increase was reduced to normal levels by additional treatment with progesterone. The investigations of Miller and Marshall, however, did not produce comparable results, and Marshall (1969) concluded that the changes in tissue catecholamine content could not account for the alteration in uterine response to nerve stimulation. Bülbring and Tomita (1968) have suggested that adrenergic action may be due to changes in the calcium binding of the muscle cell membrane, and a resulting alteration in the membrane permeability to potassium and chloride. Hence, Marshall (1969) suggests that the direction of the response may be determined by the specific membrane permeability involved, and that this, in turn, is dependent on the hormonal environment of the muscle.

Whatever the exact mechanism ultimately proves to be, there seems good evidence from the experiments reported above that the well recognised effects of œstrogen and progesterone on the ureters are pharmacological in nature, and are produced by modifying the sensitivity of the α- and β-adrenergic receptors in the ureteric muscle. In particular, a high level of progesterone, by facilitating the β-receptors, will result in hypotonicity of the ureter, as seen in pregnancy.

SUMMARY

A series of isometric studies were performed on rat ureters to investigate the effect of pre-treatment with œstrogen and progesterone on the α- and β-adrenergic responses.

The results indicate a facilitation or enrichment of the α-adrenergic response by œstrogen, and a similar effect on the β-response by progesterone.

It is suggested that the hormonal component of the ureteric dilatation of pregnancy is the result of the effect of progesterone on the β-adrenergic receptors.

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URETERAL OBSTRUCTION IN THE PATIENT WITH PROSTATIC CARCINOMA[1]

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CARCINOMA of the prostate may cause hydronephrosis and renal insufficiency. The pathogenesis is usually " . . . obstruction of the ureteral orifices by the primary tumour or compression of

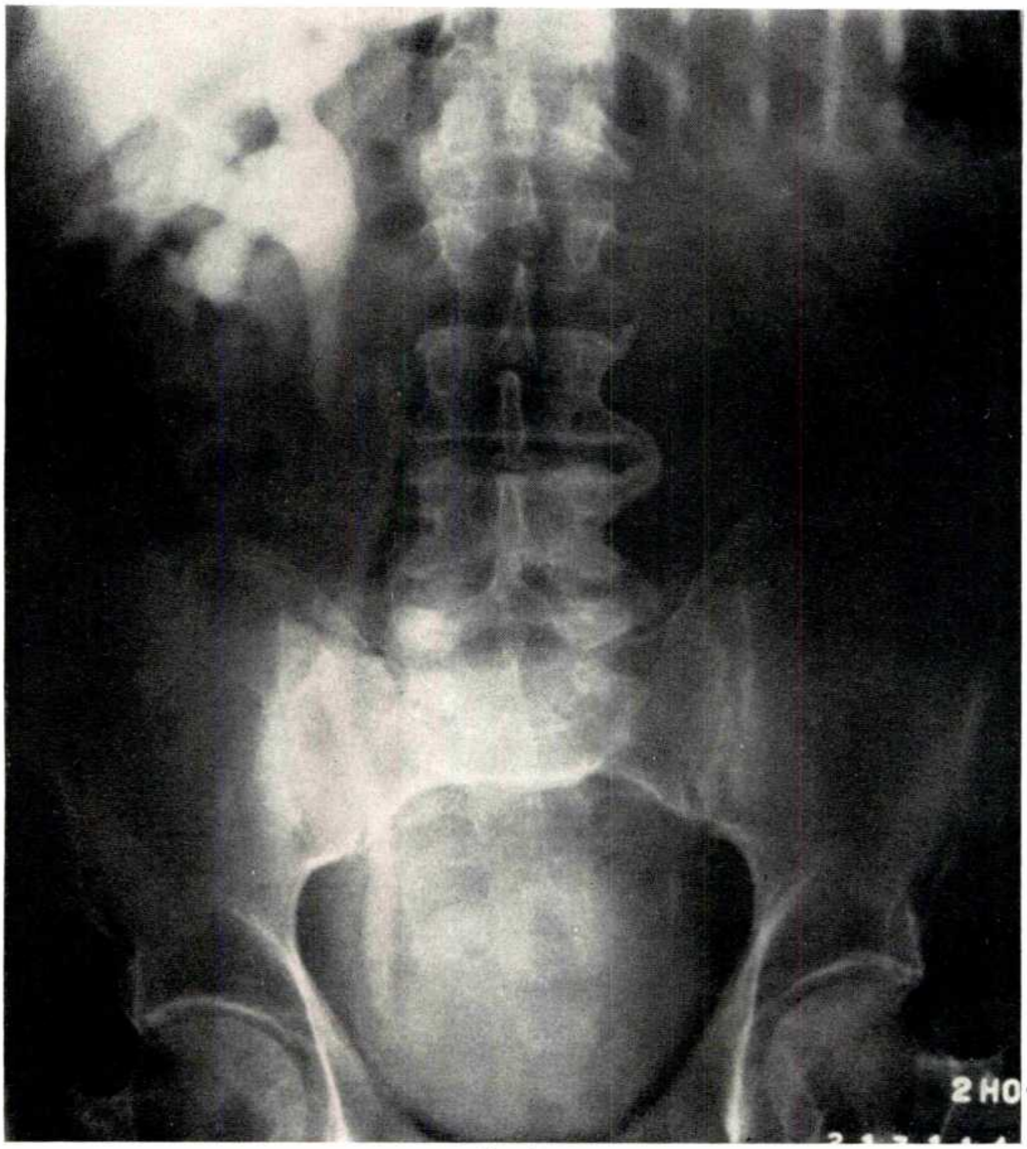

FIG. 1

Intravenous pyelogram on admission. Two hour delay film.

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[1] Presented October 30, 1971, Mid-Atlantic Section Meeting, American Urological Association, Williamsburg, Virginia.

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the ureters by masses of iliac lymph nodes involved by metastatic cancer (Smith, 1966)." A third mechanism, less commonly found than the other two, is luminal occlusion by metastasis in the wall of the ureter. Such an occurrence has been documented in the world's literature eight times since the first reported case (Giordano and Bumpus, 1922), but only once in the past 40 years (Kost and Leberman, 1965). Kost and Leberman speculate that the lesion may be more common than generally realised, considering the early lymphatic spread of this cancer.

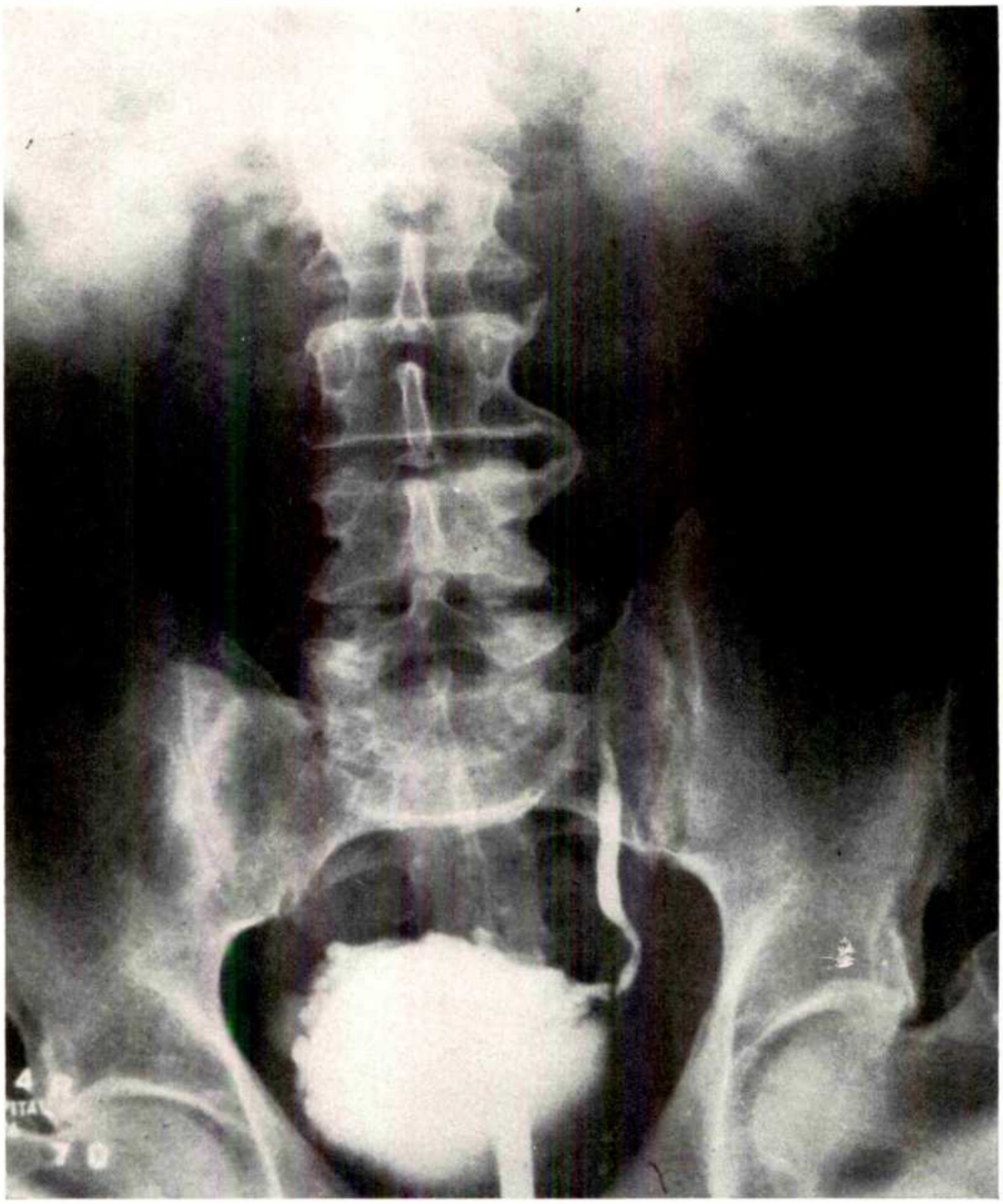

FIG. 2
Left retrograde pyelogram (performed three hours after intravenous pyelogram).

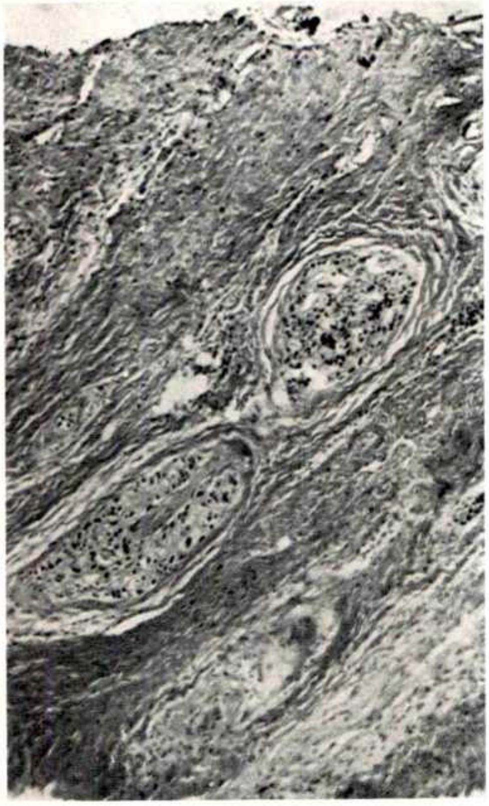

FIG. 3
Trans-rectal needle biopsy of prostate. H. & E. × 70.

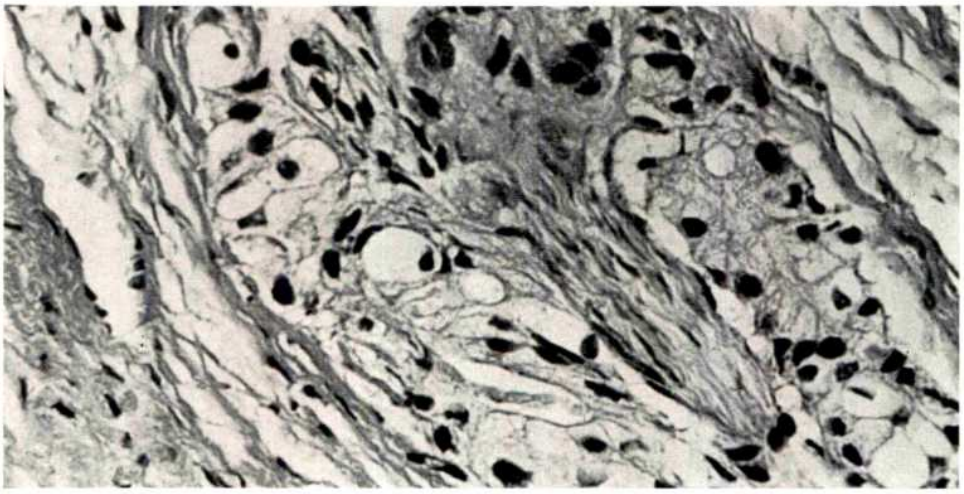

FIG. 4
Carcinomatous nodule from Figure 3, showing perinural invasion. H. & E. × 320.

Hydronephrosis secondary to carcinoma of the prostate may resolve with appropriate conservative therapy. However, ureteral metastasis from prostatic cancer has been correctly diagnosed only at necropsy or nephro-ureterectomy in all cases reported (Giordano and Bumpus, 1922; Kost and Leberman, 1965; Carson, 1925, 1927; Glas, 1926; Mackenzie and Ratner, 1932; Kirschbaum, 1933), prior to the following:

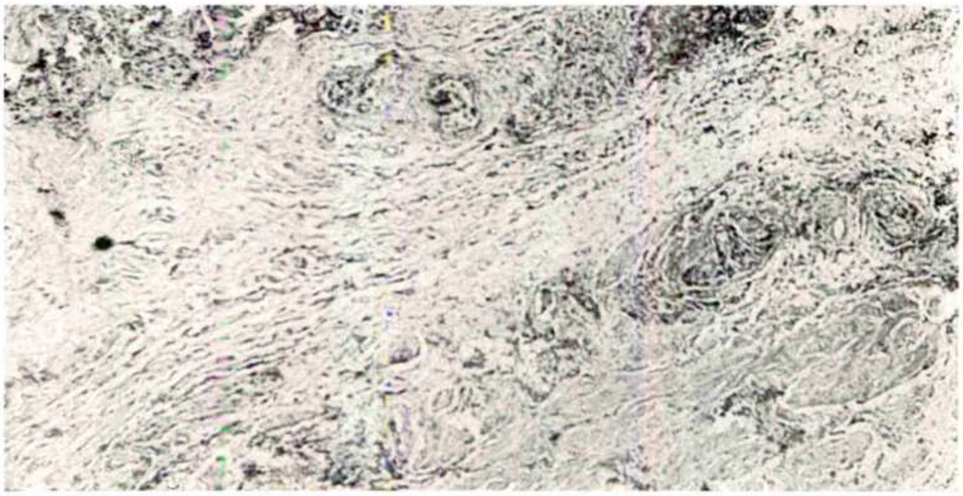

FIG. 5

Section of left mid-ureter, showing metastatic adenocarcinoma in the muscularis and adventitia. H. & E. × 70.

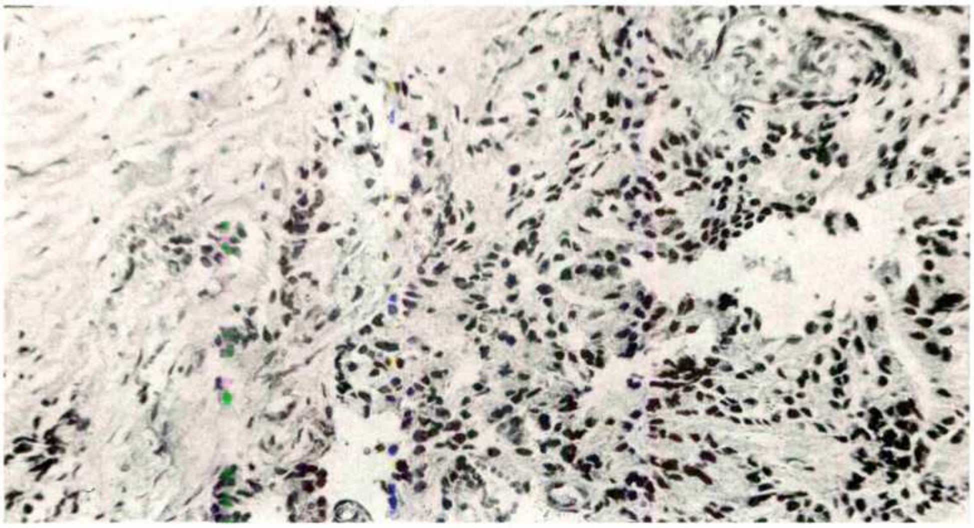

FIG. 6

Prostatic carcinoma within the wall of the ureter. H. & E. × 320.

Case Report.—A 56-year-old Caucasian seaman was admitted to the Norfolk, Virginia, U.S.P.H.S. Hospital, 21st December 1970, because of prostatism of two months' duration. The prostate gland was enlarged and very firm. The left lobe was elongated, and the gland was immobile. No hepatomegaly or lymph-adenopathy was present. Chest X-ray was normal. A bone survey was normal, except for a questionable blastic lesion involving the body of the fourth lumbar vertebra. Phosphatases on 5 different occasions were normal. The BUN was

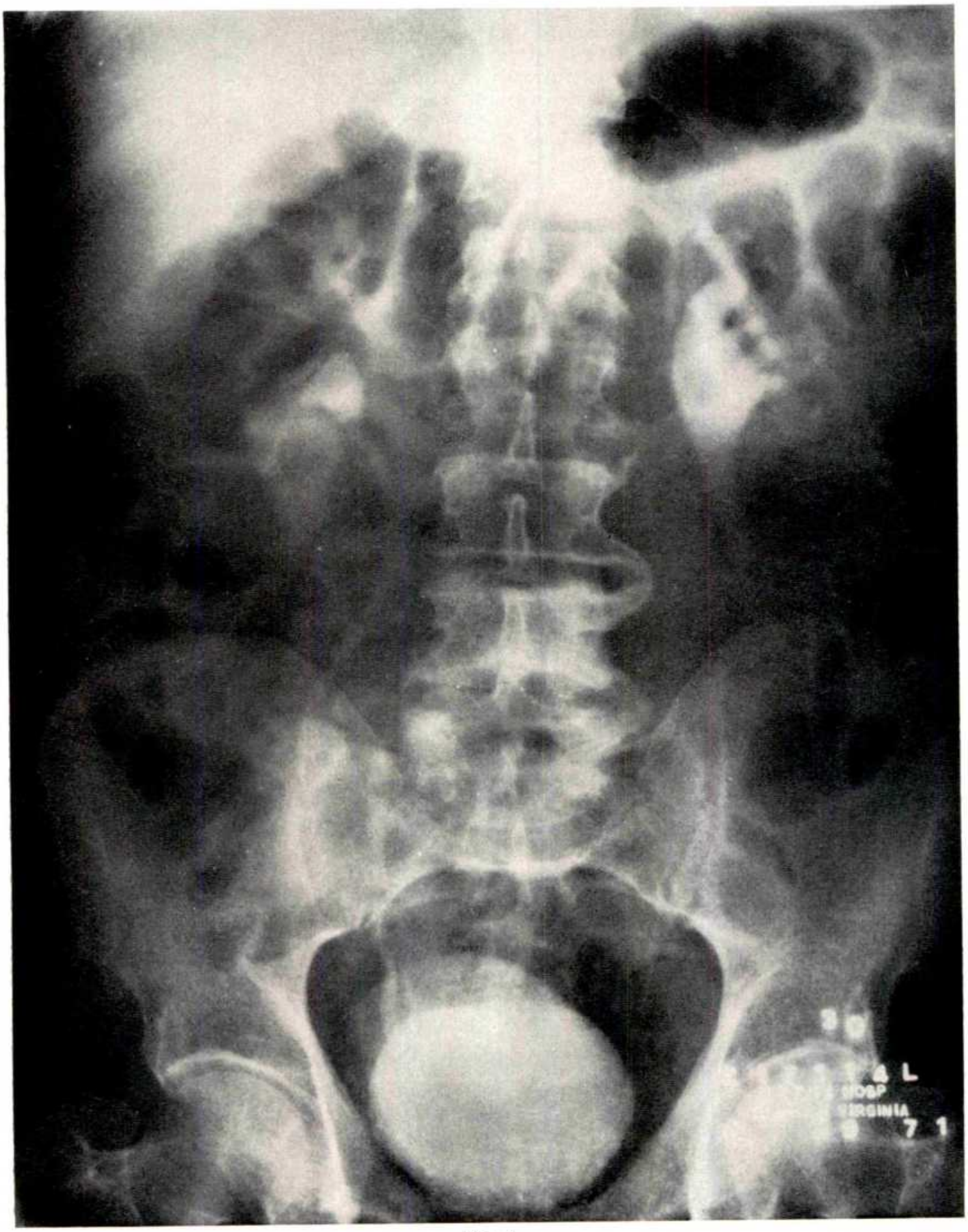

FIG. 7
Intravenous pyelogram, three months after left ureteral exploration and biopsy.

17 mg. per cent. The urine contained numerous red and white blood cells, but no casts. Excretory urography revealed the following (Fig. 1): dilatation of the right renal collecting system and ureter, with apparent obstruction at the level of the ureterovesical junction; and non-visualisation of the left kidney and ureter.

At cystoscopy the bladder appeared heavily trabeculated. Urine flowed from the right, but not the left ureteral orifice. An occlusive retrograde pyelogram was attempted (Fig. 2). Contrast material flowed approximately to the mid-portion of the left ureter, above which complete filling could never be obtained. Straight catheters could be advanced no further than this point. Trans-rectal needle biopsy was performed. Adenocarcinoma appeared in specimens taken from both right and left prostatic lobes (Figs. 3 and 4).

Castration and, subsequently, left ureteral exploration were performed. At operation the left ureter was found to be indurated near its mid-portion. No lymph nodes or direct tumour extension were found in the retroperitoneum. A biopsy of indurated ureteral wall contained metastatic adenocarcinoma (Figs. 5 and 6). The ureter was closed over a long T-tube. After the operation, estrogenic therapy was initiated intravenously and continued orally. The ureterostomy was removed on the 13th post-operative day.

A trans-urethral resection was performed for relief of prostatism, and the patient was discharged. His medications included 1 mg. of stilbestrol daily. Three months after the ureteral biopsy, excretory urography revealed grossly normal collecting systems (Fig. 7). Currently, the patient feels well and has since returned to his work.

DISCUSSION

Carcinoma of the prostate may obstruct a ureter by three different mechanisms: (1) direct extension, (2) compression by nodes, or (3) intramural metastasis, as in the present case. Distal ureteral obstruction from prostatic cancer is well known. However, middle or proximal occlusion may connote another ætiology, as it did in the case presented. Nevertheless, metastasis affects all levels of the ureter with equal frequency (Presman and Ehrlich, 1948). Several cases of carcinoma of the prostate metastatic to the ureteropelvic junction and even the renal pelvis have been reported (Giordano and Bumpus, 1922; Carson, 1927). We suggest that, regardless of the level, any ureteral obstruction in a patient with carcinoma of the prostate be attributed to the neoplasm, unless another cause is readily apparent.

First-line therapy is non-operative. The prompt disappearance of our patient's right hydro-ureteronephrosis following endocrinologic therapy supports conservative management. We can only wonder about hormonal effects on the left side, since ureterotomy complicated the result. Obstruction of the middle or upper ureter from prostatic metastasis, effectively treated without operative intervention, remains to be reported.

SUMMARY

Diagnosis and treatment of ureteral metastasis from prostatic carcinoma is discussed via an illustrative case report.

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THE FUNCTIONAL RADIOLOGY OF ECTOPIC URETEROCELE

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ECTOPIC ureterocele is an anomaly, commonly presenting in childhood, of which the diagnostic radiological features are generally well known. In summary, these are a duplex upper urinary tract with very poor function in the upper pole and an associated filling defect in the base of the bladder where there is non-opacified urine in the lower end of the ectopic ureter. This review indicates that very much more information can be obtained by additional radiological studies which permit assessment of the position and functional characteristics of the ectopic ureterocele, thereby providing a rational surgical approach to the problem.

In ectopic ureterocele the associated ureter is almost always dilated and exhibits poor contractility. Changes in the size of the ureterocele result mainly from changes in bladder pressure, and more important observations may be made from a micturating cystogram rather than from cystoscopic inspection. The effect of the ureterocele and its change in size and position upon the ipsilateral lower pole ureter and opposite ureter, as well as on the urethra, are of the greatest importance. It is to these aspects that this paper is largely devoted.

Intravenous urography broadly indicates the condition and function of the upper urinary tract. Cystography provides information about:

1. The size and position of the ureterocele.
2. Its tension and compressibility.
3. The degree to which it is backed by firm detrusor fibres.
4. Its tendency to prolapse into the urethra.
5. The degree to which it obstructs the bladder outflow.

Cystography can also distinguish cases where spontaneous or accidental instrumental rupture has occurred so that the classical signs have been altered.

The Upper Urinary Tract.—In most cases of ectopic ureterocele the ectopic ureter drains the upper pole of a duplex kidney. The size and function of the upper moiety vary considerably; commonly it is non-functioning at intravenous urography. There are exceptions where the ectopic ureter is solitary and in these the single renal element which it drains is commonly aplastic, but one such case in our series had a functioning but severely hydronephrotic kidney.

Where there is a duplex system the upper pole of the duplex is always more severely damaged than the lower pole. The upper will occasionally concentrate the opaque medium sufficiently to define the calyces, pelvis and upper ureter and the higher the dose of contrast medium and the more prolonged the examination the more likely is this to be seen. In such cases it is possible to obtain direct evidence of the degree of dilatation and motility of the ectopic ureter, but in most, where the upper pole is not opacified, its presence and dilatation must be surmised from the appearances of the lower pole.

The anatomical features which make this diagnosis possible are well known. The calyces are fewer in number than normal (Fig. 1) and the uppermost calyx is too far from the upper limit of the renal outline. The opacified calyces in the lower pole appear to be rotated downward and outwards and the highest calyx is short, sometimes suggesting mal-rotation (Fig. 2). The opacified renal pelvis is displaced away from the vertebral column and the ureter may form with the pelvis a gentle curve, gradually approaching the para-vertebral region at the level of the fourth or fifth lumbar vertebra (Fig. 3). The opacified ureter being adherent to an unseen dilated ureter is not straight but may exhibit a series of scalloped curves. The degree of dilatation of the upper pole can be surmised from the degree of displacement of the lower pole. Occasionally the upper pole ureter is so enormously dilated as to present as a large palpable mass in the abdomen and radiologically it may then be seen to compress part of the bladder (Fig. 4).

The lower pole of the kidney may be normal. It may, however, be pyelonephritic in association with reflux or it may be hydronephrotic and damaged even to the point of non-function by obstruction, either at the uretero-vesical junction or at the bladder outflow. The contra-lateral ureter may be similarly affected. These changes are usually a consequence of the features of the ureterocele to be described below, but they may be due to intrinsic ureteric disorders and it is only by careful study of the functional changes in the cystogram that an accurate diagnosis can be made and a plan for surgical treatment formulated.

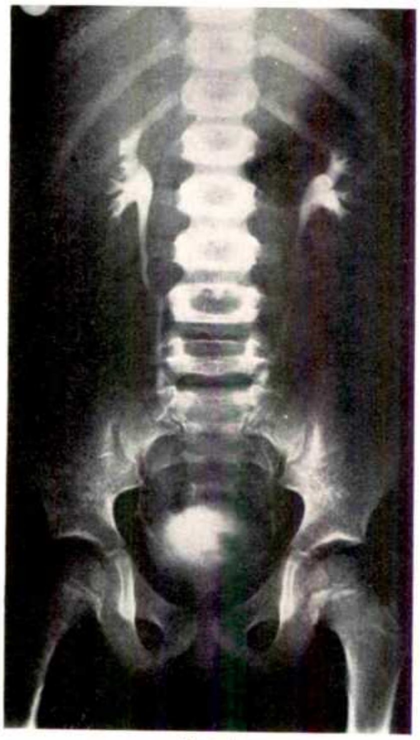


FIG. 1

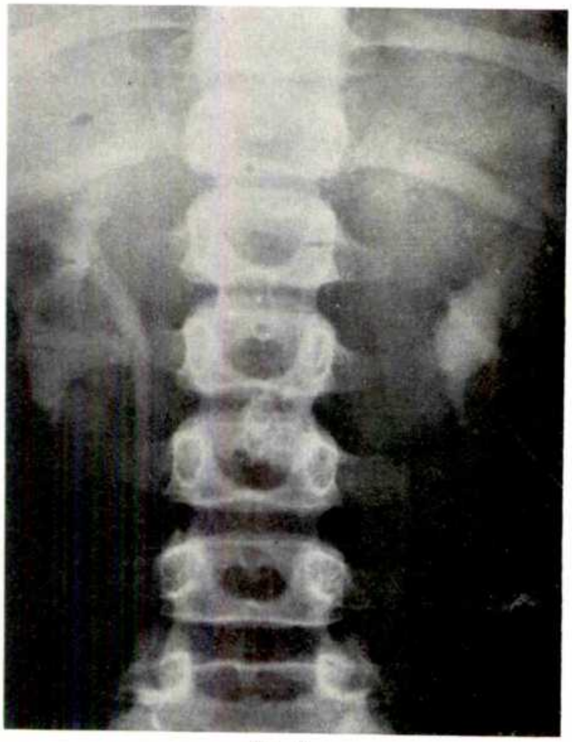


FIG. 2

Fig. 1.—I.V.P. in girl with left duplex kidney and non-opacified ectopic upper pole ureter. The visible calyces on the left are few in number, the uppermost is displaced laterally.

Fig. 2.—I.V.P. in girl with left duplex kidney and non-opacified upper pole ectopic ureter. The visible calyces on the left are far from the renal outline of the upper pole, the lower pelvis is mal-rotated.

Size and Position of Ureterocele.—The opening of the ectopic ureter is at or below the bladder neck: the ureterocele is the dilated segment within the bladder. The ureterocele varies in size and position as shown in Figure 5. It is sometimes a simple spherical sac (see Figure 4), sometimes a coiled dilated tube giving it a somewhat loculated appearance in the cystogram which could be mistaken for a bilateral condition or even a tumour (Fig. 6). Cystographically the filling defect due to an ectopic ureterocele is always based on the bladder outline and never appears, as does the orthotopic ureterocele, as a complete circle within the bladder shadow. The size of the filling defect varies considerably according to the size of the ureterocele and the degree to which it is prolapsed or compressed at the time of examination. A few are so small (Fig. 5B) that they produce only an inconspicuous crescentic bite out of the bladder neck outline. In such cases they are overlooked as attention is concentrated upon other pathology, particularly reflux into the ipsilateral lower renal pelvis due to an intrinsic defect of the lower pole ureter at its junction with the bladder (Fig. 7).

Occasionally the ectopic ureter exhibits not only the ureterocele dilatation within the bladder but a second saccular dilatation lying posterior to the urethra stretching out and partially obstructing the supra-montanal segment in the male (Fig. 5C) or the entire urethra in the female. The presence of this second post-urethral sac is only clearly demonstrated when it is filled with opaque medium and occasionally this does occur by reflux from the urethra, but in other circumstances (Fig. 8) it can be surmised from the urethral deformity and sometimes clinically in the female by the appearance of a pseudo prolapse alongside the urethral meatus.

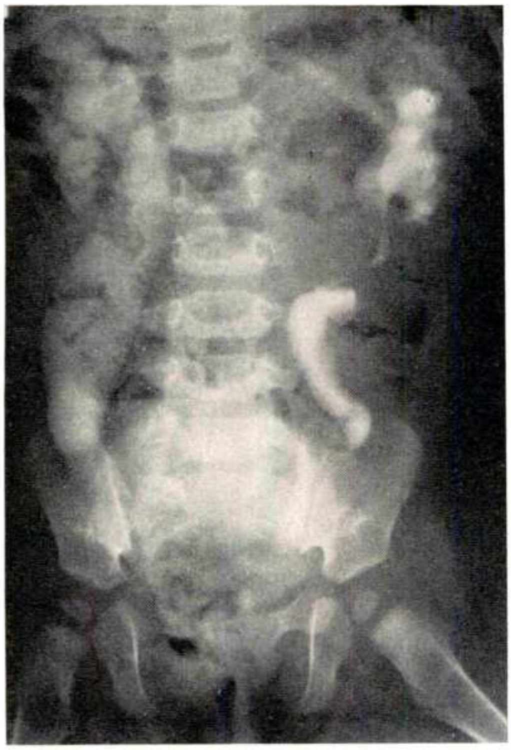


FIG. 3

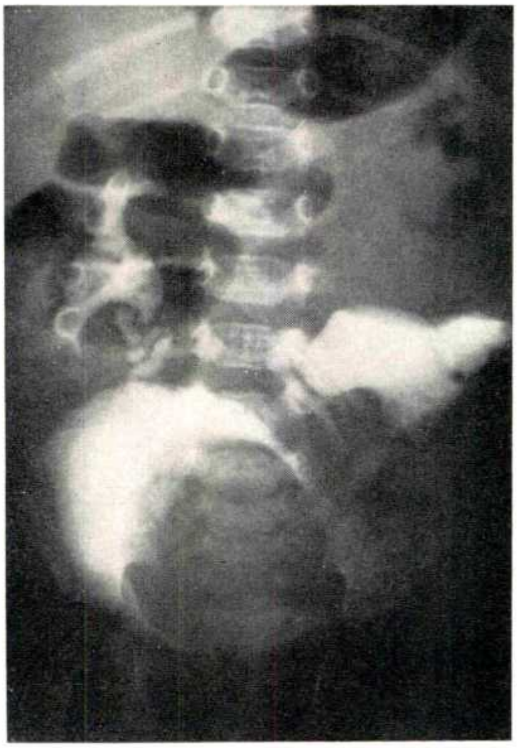
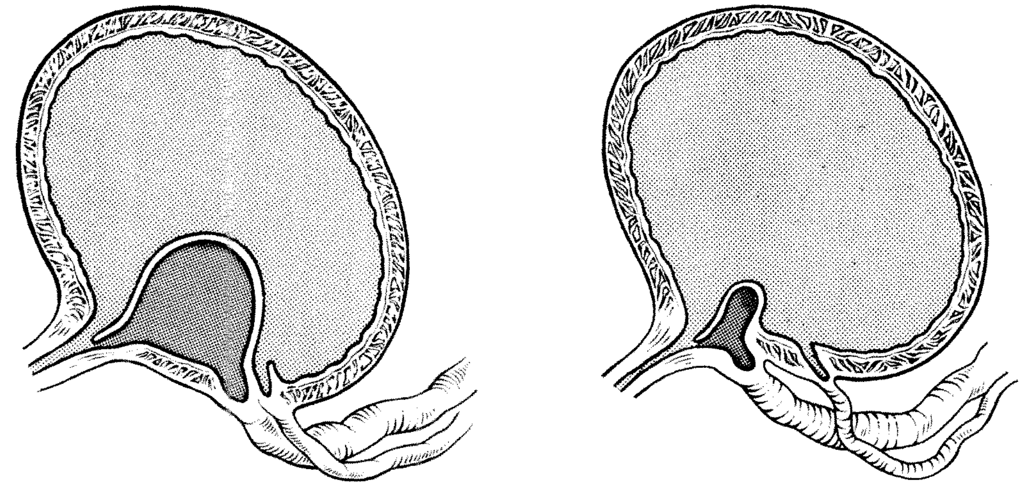


FIG. 4

Fig. 3.—I.V.P. in a girl with left duplex kidney and non-opacified ectopic upper pole ureter with ureterocele. The visible renal pelvis is displaced laterally and tipped downwards, the visible ureter lies in curves around the unseen dilated ureter.

Fig. 4.—I.V.P. in a girl with left duplex kidney and non-opacified ectopic upper pole ureter with ureterocele. Enormous dilatation of the unseen upper renal element and ureterocele filling defect in the bladder.

Tension and Compressibility.—The degree to which the ectopic ureterocele varies in size during the act of micturition varies greatly from one case to another depending upon its compressibility and an attempt should always be made to estimate this variability during micturating cystography. To obtain a good view of the ureterocele the opaque medium should not be too dense. In our series 35 per cent Diodone diluted with an equal volume of normal saline was used. Films should be exposed in the oblique or lateral planes both in the early and late stages of bladder

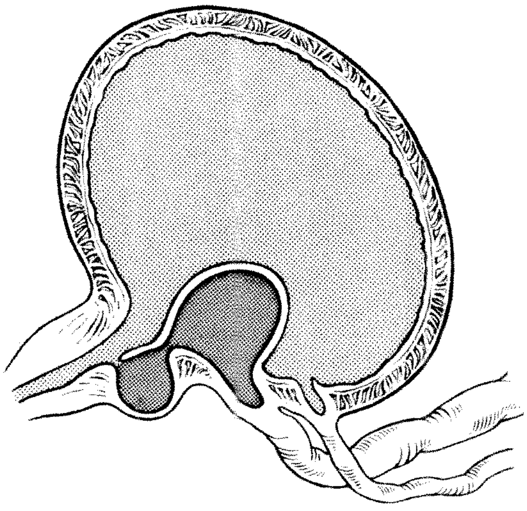


Classical ectopic ureterocele

A, The classical form.

Ectopic ureterocele variant

B, Small variant.



Ectopic ureterocele variant

C, Variant with retro-urethral sacculation.

FIG. 5
Diagrammatic anatomy of ectopic ureterocele.

filling as well as during micturition. Observations must be made upon the urethra and ureteric reflux as well as upon the size and position of the ureterocele.

The tension within the ureterocele presumably depends upon the severity of the obstruction at the ectopic orifice. If the obstruction is virtually complete it is likely that the ureteric contents will be under high pressure whatever the function of the associated renal element. This tension will be increased during infections with obstructive œdema at the orifice. The tense ureterocele remains approximately the same size during micturition (Figs. 9 and 10) and the filling defect which it produces has often a nearly circular outline. By contrast, where the ectopic orifice is wide and the contents of the ureter held at low pressure the ureterocele is compressed during micturition and its contents empty back up into the ureter, or down into the urethra (Figs. 11, 12 and 13).

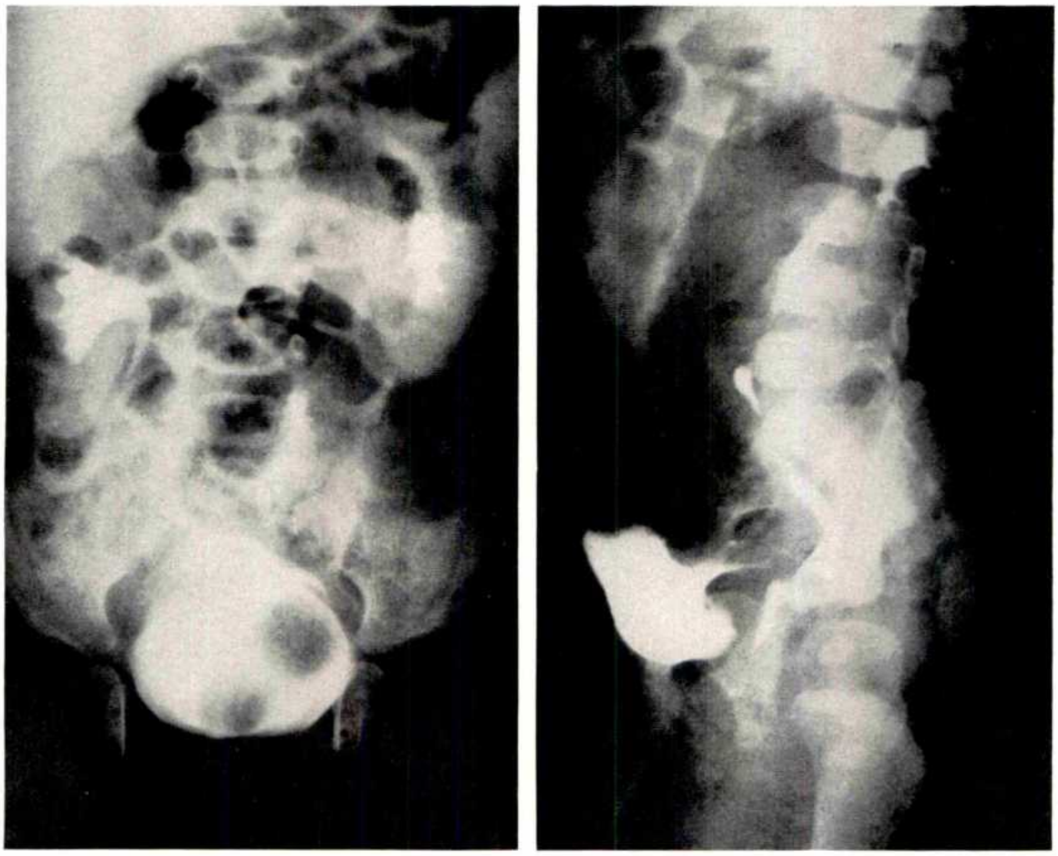


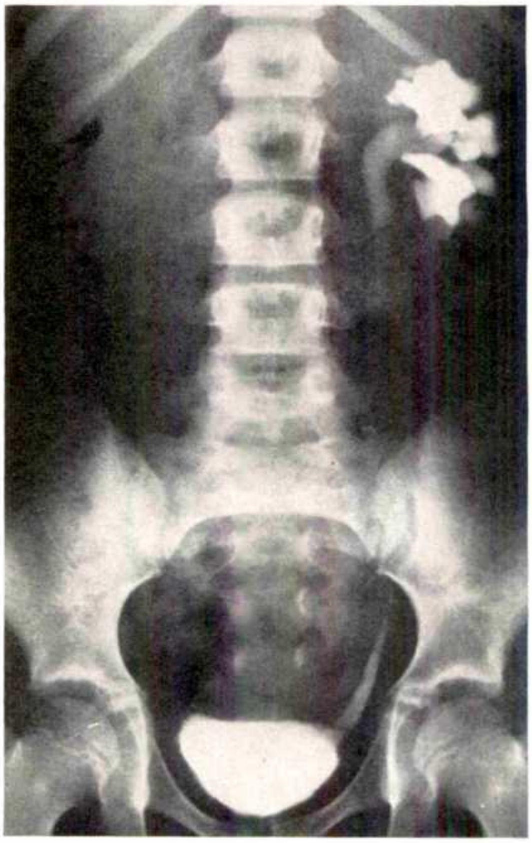
FIG. 6

A, I.V.P. in a girl with bilateral duplex kidney: on the right there was a simple urethral ectopic ureter, on the left an ectopic ureterocele formed by a tortuous dilated ureter beneath the vesical mucosa. B, Lateral view in the same case showing the posterior projection of the bladder cavity forming the upper part of the circumferential sulcus around the ureterocele.

In the case of the tense ureterocele the ipsilateral lower pole ureter is drawn up on to its surface; this gives it a long sub-mucous course which is compressed against the tense ureterocele during micturition and it is therefore valvular, it does not allow reflux and in such cases the ipsilateral lower pelvis will be either normal or hydronephrotic. The contra-lateral ureter may be similarly affected.

With the compressible ureterocele during micturition the ipsilateral lower pole is not stretched up, it has a lax support and no valvular action. Reflux is therefore likely. If infection has been present pyelonephritic scarring will then accompany reflux in the lower pole of the kidney. A review of a series of our cases in which adequate data were available (Table I) shows this clear correlation between the presence and absence of reflux and the compressibility or otherwise of the ureterocele. It must be noted that in either case reflux may occur post-operatively if the ureterocele is simply uncapped for then the lower pole ureter is no longer supported.

Good Backing and Poor Backing.—In some cases the ectopic ureterocele is entirely within the bladder and an almost normal sheet of detrusor muscle is present behind it; this can sometimes be seen in the outline of the ureterocele on the cystogram, or it can be observed even more satisfactorily if the ureterocele itself is filled with opaque medium while the bladder is filled with water (Fig. 14). In other cases the detrusor coat posteriorly is poor and may even in a few be absent (Fig. 15): this condition is defined as " poor backing " and there is, of course, a gradation between ectopic ureteroceles with good backing and those with poor backing—indeed, a further gradation to cases of ectopic ureter with a dilated segment lying entirely outside the detrusor coat. During micturition cystography those with poor backing may be demonstrably displaced outwards as shown by the position of the " circumferential sulcus ". This term is applied to the gutter formed where the mucous membrane of the bladder is reflected on to the ureterocele (Figs. 6A and B): as the bladder contracts the opaque medium in the fundus has a crenellated outline corresponding to the trabeculation of the bladder wall, but in the bladder base the ureterocele remains smooth with only a thin layer of opaque medium around it. This layer opacifying the circumferential sulcus may appear within the general outline of the bladder if the detrusor backing



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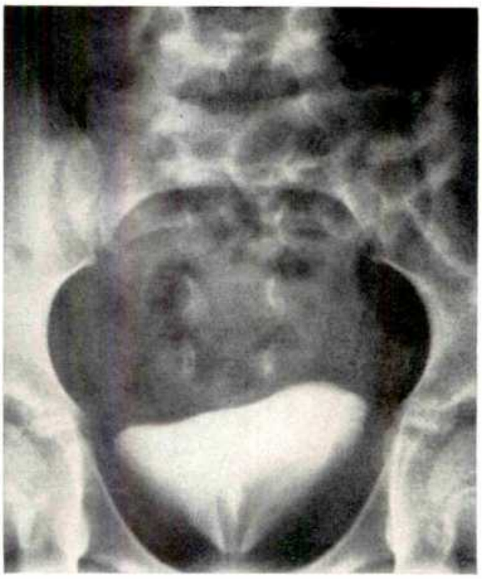
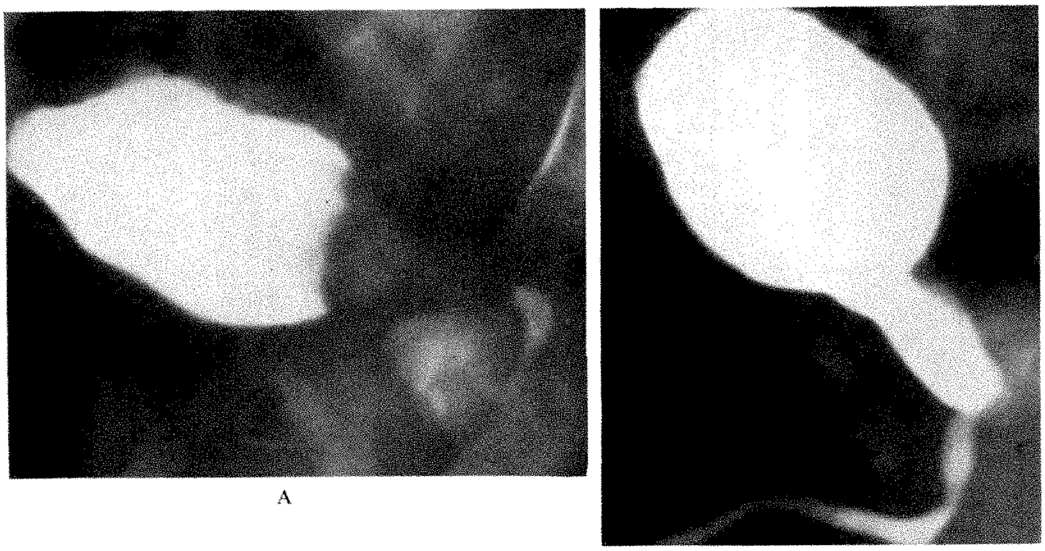


B

FIG. 7

A, Cystogram in a girl with left duplex kidney and ectopic upper pole ureter and ureterocele. Free reflux into the lower pole, which is pyelonephritic: ureterocele is obscured by the density of the opaque medium in the bladder. B, I.V.P. films of the bladder in the same case. The defect of the ectopic ureterocele can be seen as a triangular area in the base of the bladder.



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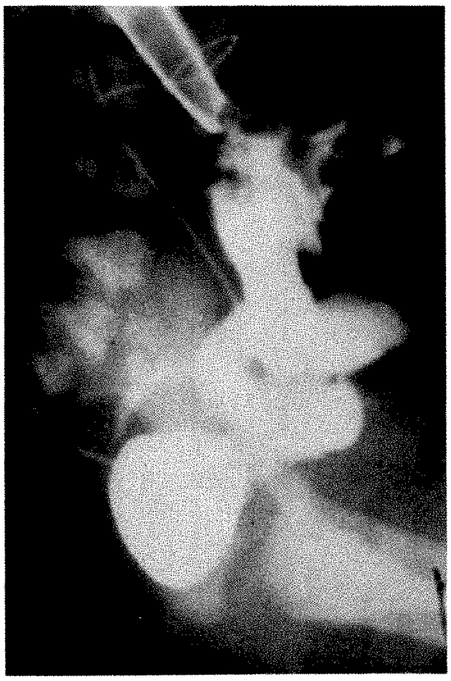


C

Fig. 8

A, Cystogram in a male infant with bladder outflow obstruction showing a filling defect in the base of the bladder. B, Micturition films in the same series: the ureterocele is now obscured by the density of the opaque medium but the elongation of the supra-montanal urethra is demonstrated. C, A ureterogram at operation, the enormous loculated ureterocele is filled, no opaque medium enters the bladder or urethra.

is good (Fig. 16) or may be displaced widely outside the expected outline if the backing is poor (Fig. 17).

The nature of the backing determines the choice of operation. The ureterocele with good backing may be uncapped within the bladder leaving a smooth wall which is well supported. Post-operatively cystograms will then show no deformity of the normal vesical outline. However,

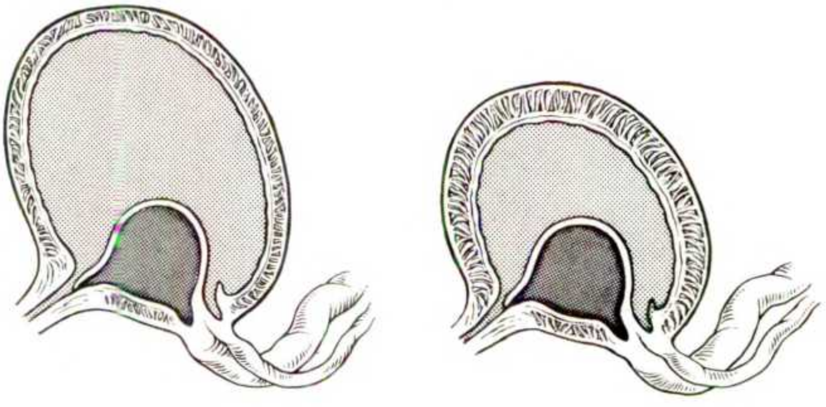
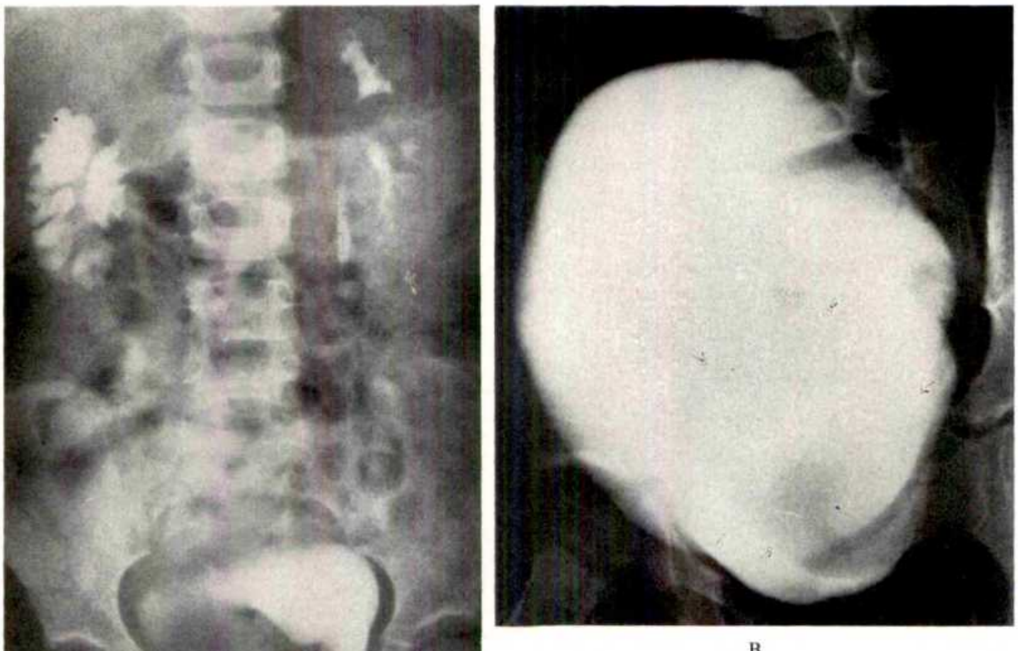


FIG. 9

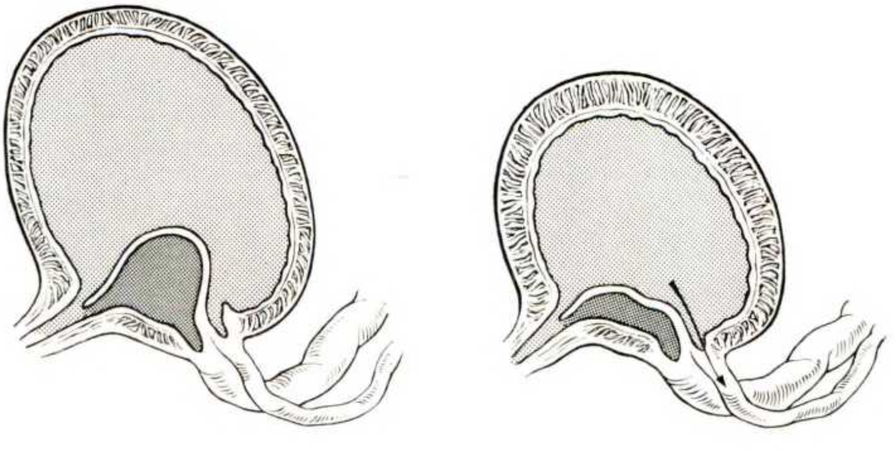
Diagrammatic view of the tense ectopic ureterocele. It does not alter in size during micturition and the ipsilateral lower pole ureter remains drawn up on to its slopes with a long sub-mucous course which is valvular and does not allow reflux, although it may cause obstruction.


B

A

FIG. 10

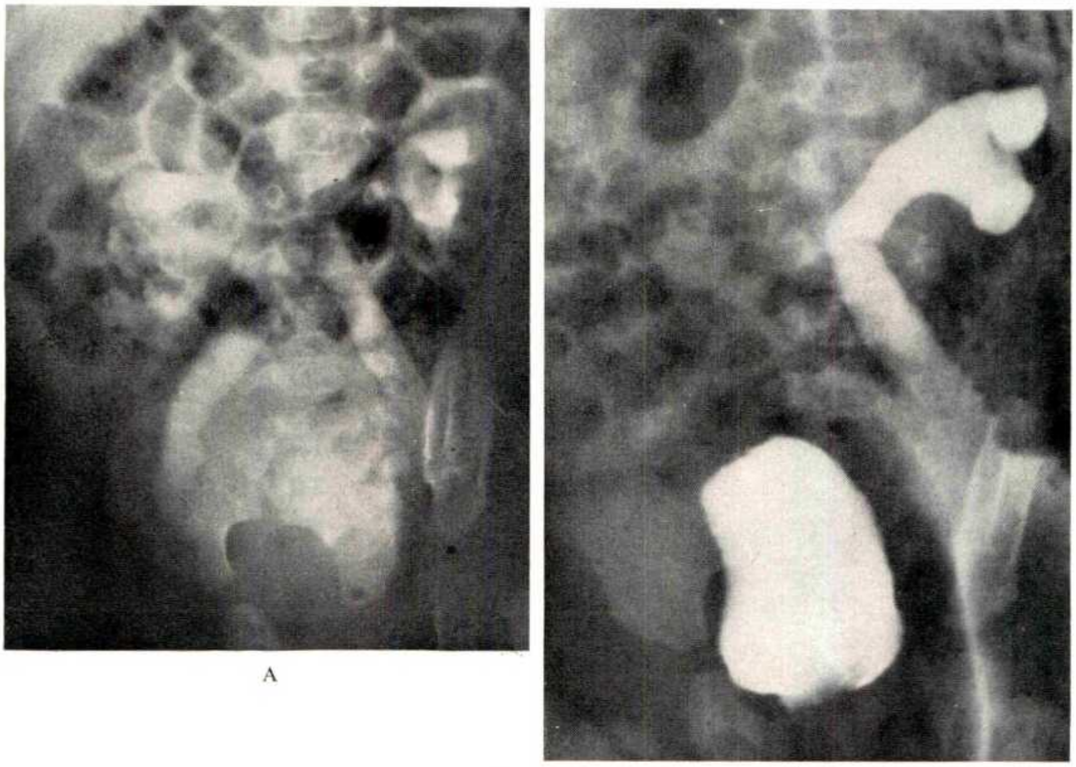
A, I.V.P. in a girl with right duplex kidney and non-opacified upper pole ectopic ureter with tense ureterocele. B, Cystogram in the same case: the ureterocele does not alter in size during micturition. No reflux occurs but obstruction is caused to the ipsilateral lower pole ureter.



Compressible ectopic ureterocele with strong bladder backing

FIG. 11

Diagrammatic view of compressible ectopic ureterocele: it collapses during micturition and the ipsilateral lower pole ureter is no longer supported, reflux therefore occurs.

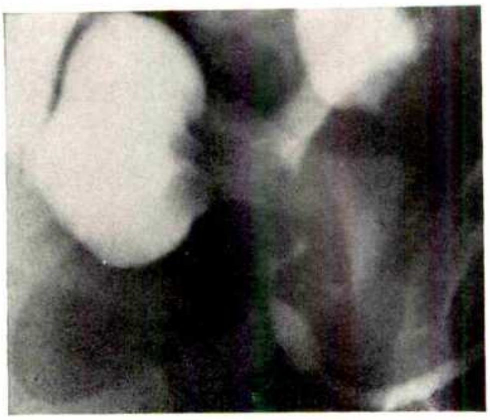


A

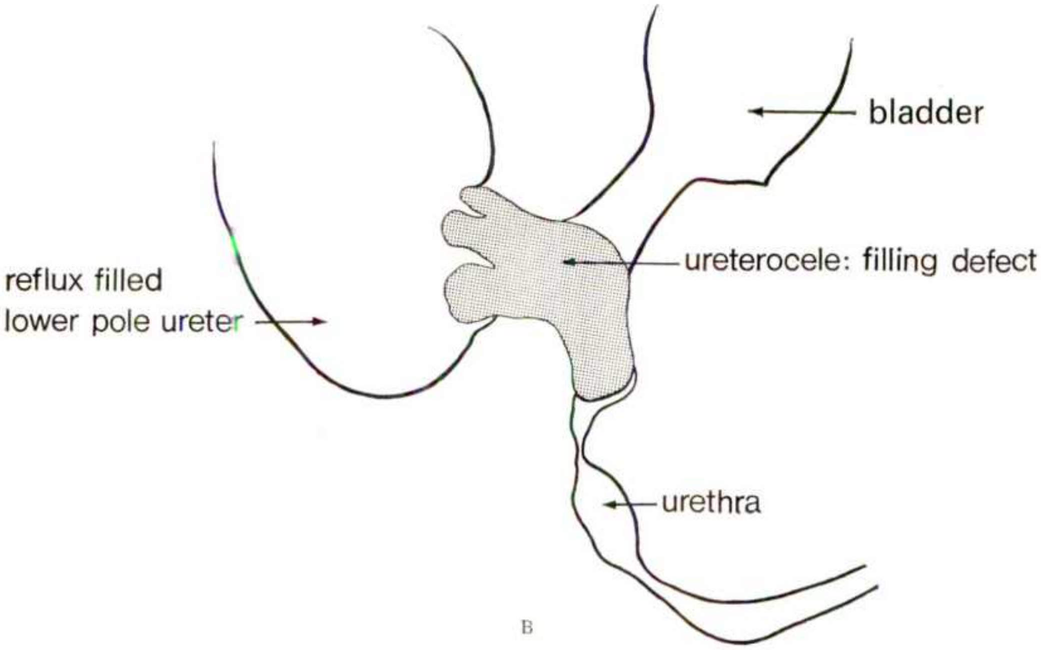
B

FIG. 12

A, I.V.P. in a boy with left duplex kidney and non-opacified ectopic upper pole ureter with compressible ureterocele. B, Cystogram in the same case shows that the large filling defect in the pyelogram is replaced by a small irregular defect at the bladder base during micturition. Reflux occurs into the ipsilateral lower pole.



A



B

FIG. 13

A, Cystogram of a boy with left duplex kidney and ectopic ureterocele. The micturating films show the contracting bladder, the crumpled filling defect of the compressible ureterocele and reflux into the ipsilaterallower pole ureter (no reflux into the ectopic ureter). B, Explanatory diagram.

TABLE I

Associated Complications of 34 Cases of Ectopic Ureteroceles

Type of ureterocele	Total no. of cases	Reflux				Bladder wall		Hydronephrosis			
		None	Ipsi	Contra	Bilat	Weak	Strong	None	Ipsi	Contra	Bilat
Tense	11	11	—	—	—	1	10	2	5	—	4
Compressible	18	4	12	2	1	5	14	2	10	—	7
Ruptured	5	—	5	—	—	2	3	1	2	1	1

in the case of the ureterocele with poor backing, if a simple uncapping is performed there is a weak area in the trigone forming a broad based bulge at rest which blows out considerably on micturition, sometimes throwing up an obstructive distal lip at the bladder neck or urethra. In such a case complete excision of the entire terminal ureter with the adjacent bladder wall and reconstruction of the detrusor coat is the proper treatment, even though this is a much more considerable operation.

Prolapsing Ureterocele.—The majority of ectopic ureteroceles end at or slightly below the bladder neck and do not alter their position significantly during micturition, although they may be tense or compressible. Some, however, prolapse into the urethra either chronically or intermittently (Figs. 18 and 19) during acts of micturition. In the girl the prolapsed portion will appear at the external urinary meatus and the diagnosis can be made clinically.

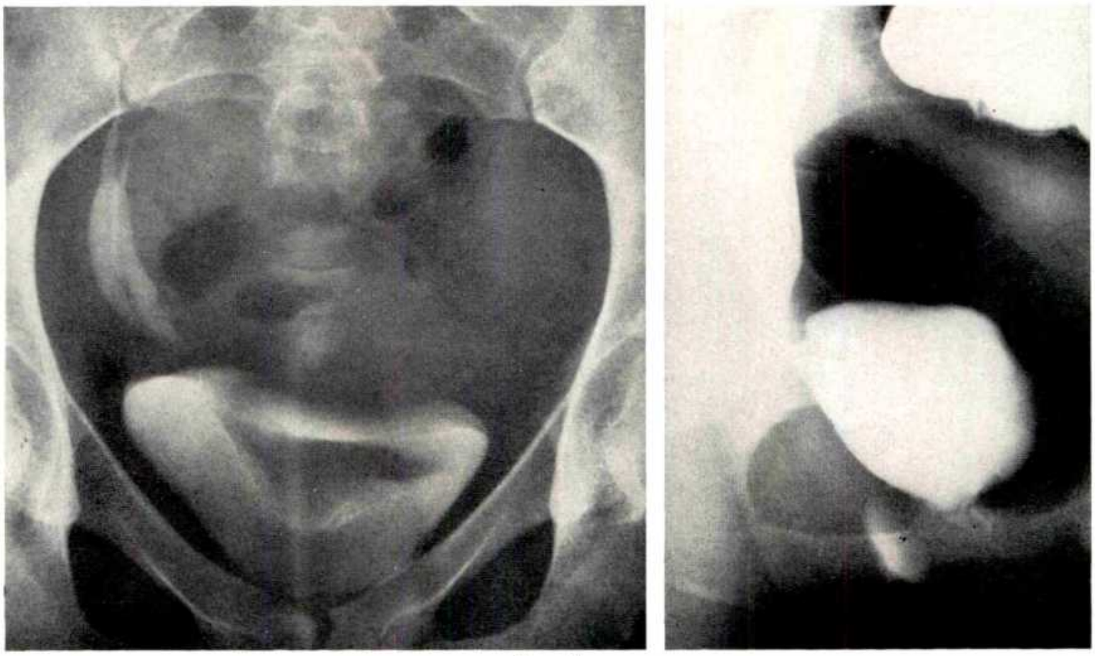


FIG. 14

A, I.V.P. B, Descending ureterogram in a girl with compressible ureterocele with good " backing " of detrusor fibres. Distention of the ureterocele occurs only forwards into the bladder.

It must be recognised, however, that the cystogram of a prolapsed ureterocele can be misleading since the characteristic filling defect is not present in the bladder itself and the deformity of the urethra can be very hard to interpret. In the male the ureterocele cannot prolapse beyond the membranous urethra, but a partial prolapse will produce a cone-shaped dilatation of the posterior urethra (Fig. 20). It is important to recognise that the obstruction here is due to the prolapse and not to a urethral stricture or to posterior urethral valves. If the opaque medium is too dense the ureterocele itself may be missed on cystography. A repeated prolapse may lead to necrosis of the ureterocele and ultimately to spontaneous rupture.

Bladder Outflow Obstruction.—The obstructive effect of a ureterocele varies considerably from one case to another and the precise factors concerned are not always apparent. A very large ureterocele may permit normal bladder emptying while a small one may be obstructive.

Obstruction may occur in both sexes, but the most severe degrees of detrusor hypertrophy are seen in the male, particularly where there is a relatively small ureterocele which is not compressible but which prolapses into the posterior urethra. In such cases there may be severe dilatation of the ipsilateral lower pole ureter and contra-lateral ureter comparable to that seen in urethral valves and as likely to persist after the removal of the primary obstructive factor. Thus some of the most severe examples of upper tract dilatation have been seen in children with ruptured ureteroceles, and it is then only by careful radiological studies that the diagnosis of the original cause of the condition can be established.

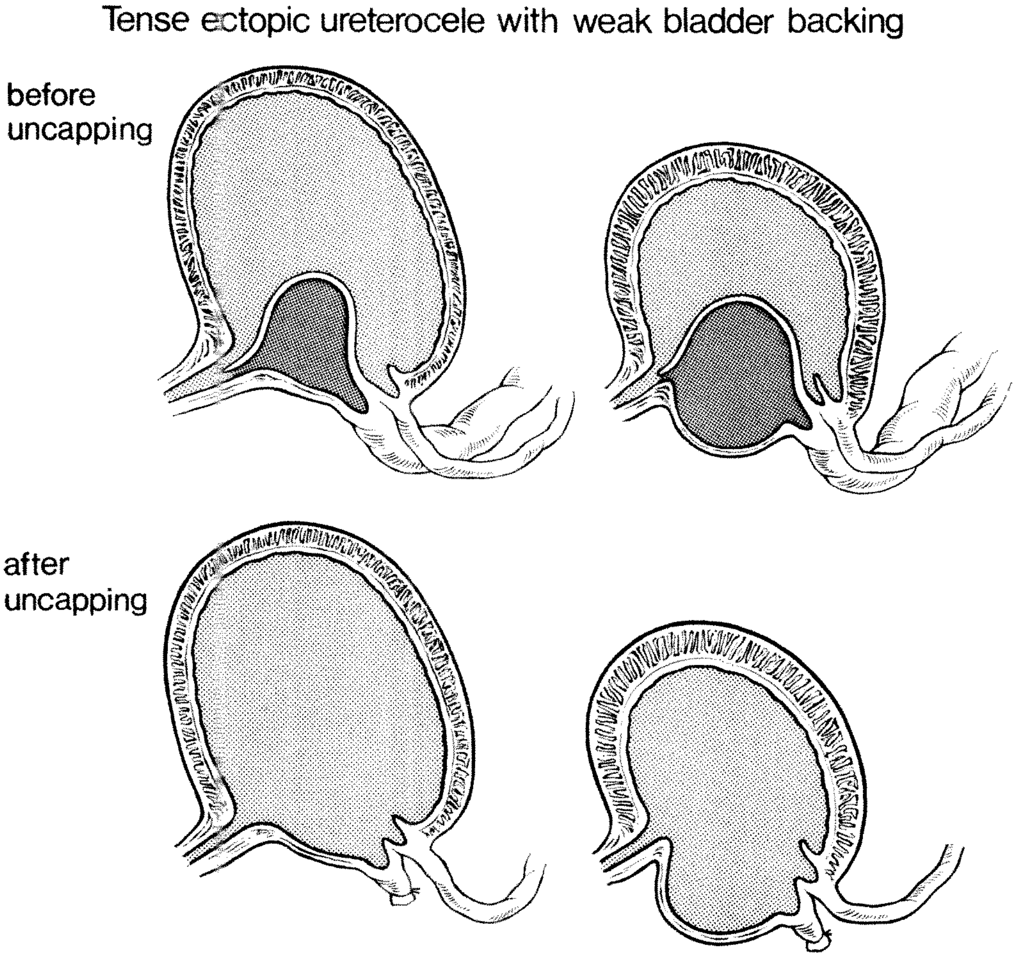


FIG. 15
Diagrammatic view of ectopic ureterocele with poor " backing ". It is displaced outwards during micturition. After a simple uncapping operation the poor backing results in a wide-mouthed diverticulum which during micturition blows out and throws up an obstructive lip at the bladder neck.

Ruptured Ureterocele.—Spontaneous rupture of the ureterocele may occur particularly if it has prolapsed and become necrotic (Fig. 21). At other times a simple instrumentation may lead to rupture even before the diagnosis is made. It is important to recognise the radiological appearance of the ruptured ureterocele, which is seen as an irregular cavity just outside the outline of the bladder and possibly with a free edge forming an irregular filling defect within the bladder shadow (Figs. 22 and 23). Characteristically, on micturition reflux occurs both into the ectopic ureter and into the unsupported ureter from the ipsilateral lower pole.

There is a further complication of a ruptured or uncapped ureterocele. Some children, where the ectopic ureter originally opened very low down the urethra, developed a " double channel " incontinence. Urine from the bladder can pass down the urethra or can escape through the distal end of the ectopic ureter and is uncontrolled by bladder neck musculature. This can be demonstrated by very careful cystography, although it is hard to obtain the film in the exact plane which shows the two channels, which are extremely close to one another. Recognition of this form of incontinence is of vital surgical importance, however, since it demands a radical removal of the ectopic ureter channel together with a reconstruction of the posterior wall of the urethra and bladder neck.

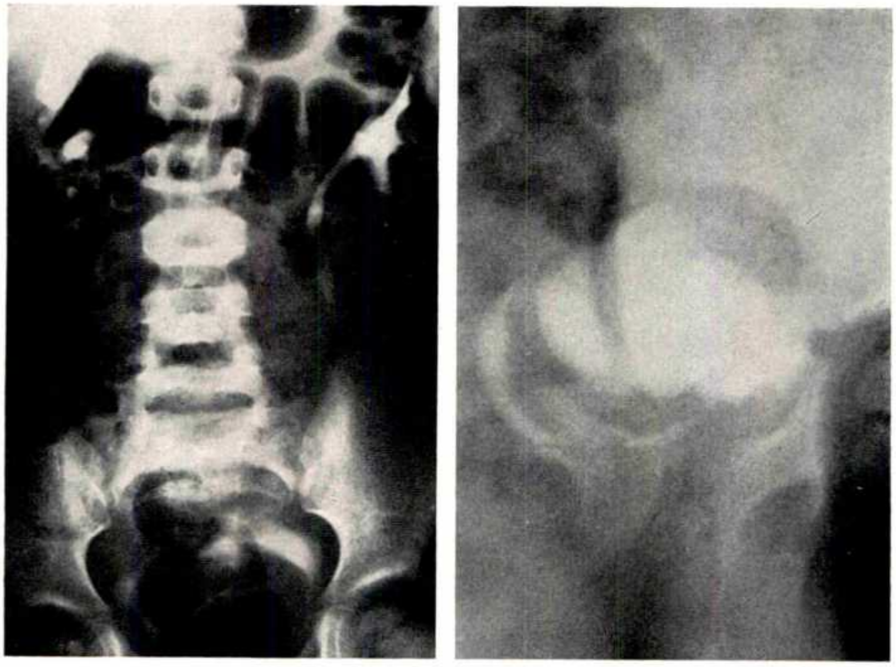
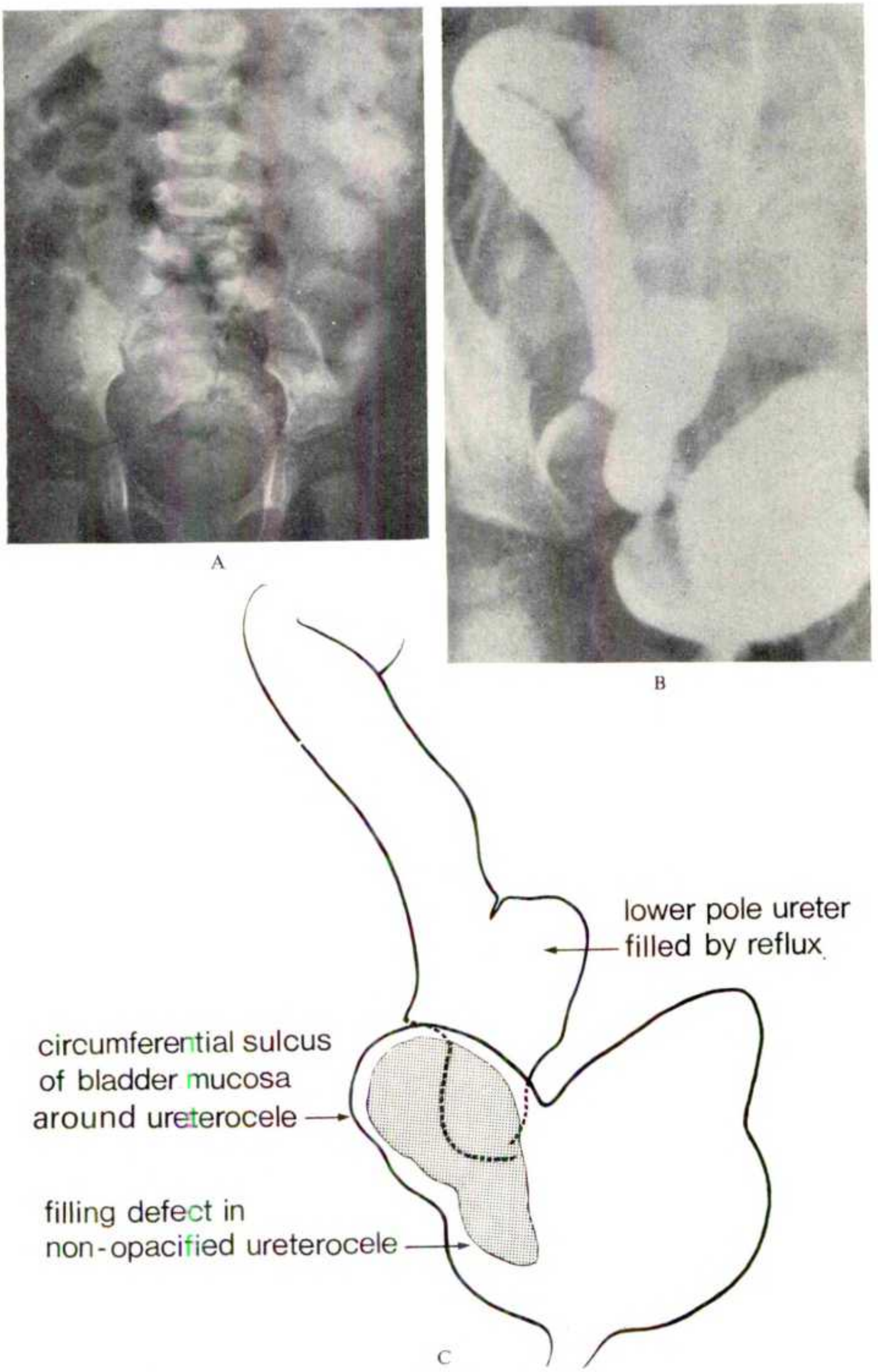


FIG. 16

A, I.V.P. in a boy with bilateral duplex and non-opacified left upper pole ectopic ureter with tense ureterocele. B, Cystogram showing the irregular shadow of the contracting bladder on the right of the film and at the bladder base the filling defect of the ureterocele surrounded by the circumferential sulcus filled with opaque medium. In this case detrusor backing is good and the sulcus appears more or less in line with the rest of the bladder outline.

SUMMARY

Ectopic ureterocele is a common condition in pædiatrics, which can, in general, be recognised from a standard intravenous urographic series. The full potential of radiological diagnosis is seldom exploited, however, and this paper gives examples of ways in which careful studies of micturating cystograms can give precise information about the nature and complications of the ureterocele, which are essential for rational planning of surgical treatment.



A

B

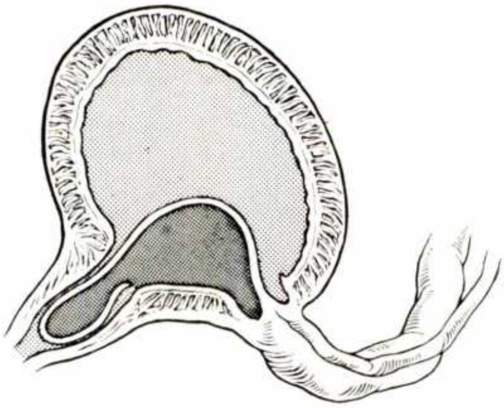
C

FIG. 17

A, I.V.P. in a boy with right duplex kidney and non-opacified ectopic upper pole ureter with ureterocele. The lower pole on the right is also severely damaged by hydronephrosis and does not opacify either. B, Cystogram showing the contracting bladder with reflux into the right lower pole ureter, the filling defect of the ureterocele and the circumferential sulcus displaced far out from the normal bladder outline. C, Explanatory diagram.

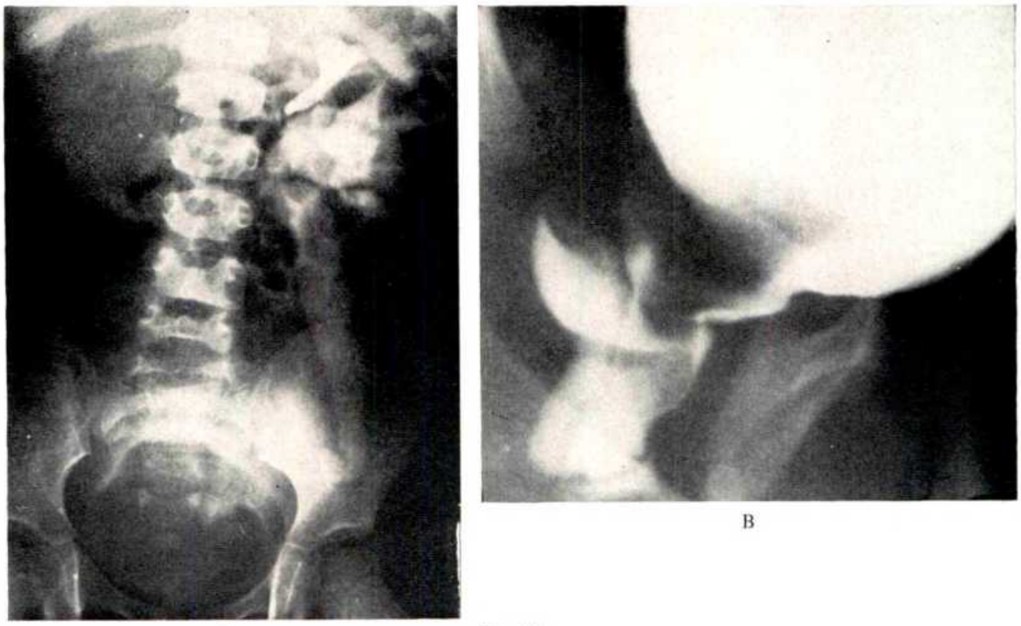
Fig. 18.—Diagrammatic view of prolapsing ectopic ureterocele.

Fig. 19.—A, I.V.P. in a girl with bilateral duplex kidney and non-opacified right upper pole ectopic ureter with ureterocele. Non-opacified lower pole on the right and obstructed kidney on the left. B, A micturating cystogram shows the filling defect of the ureterocele which is tense and alters very little in size during micturition but is partly displaced into the upper portion of the urethra producing a filling defect there. Some opaque medium has also flowed into the vagina.



Prolapsed ectopic ureterocele with strong bladder backing

FIG. 18



A

B

FIG. 19

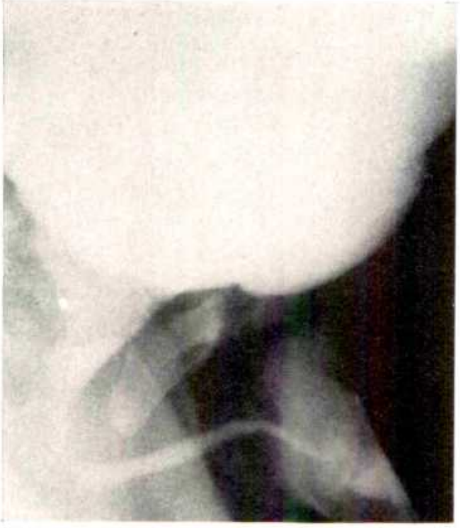


FIG. 20

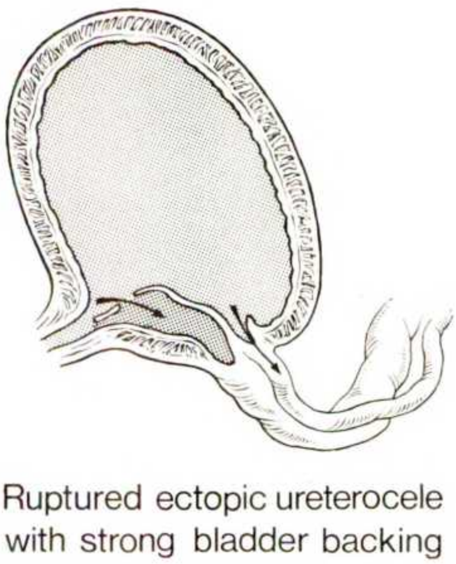
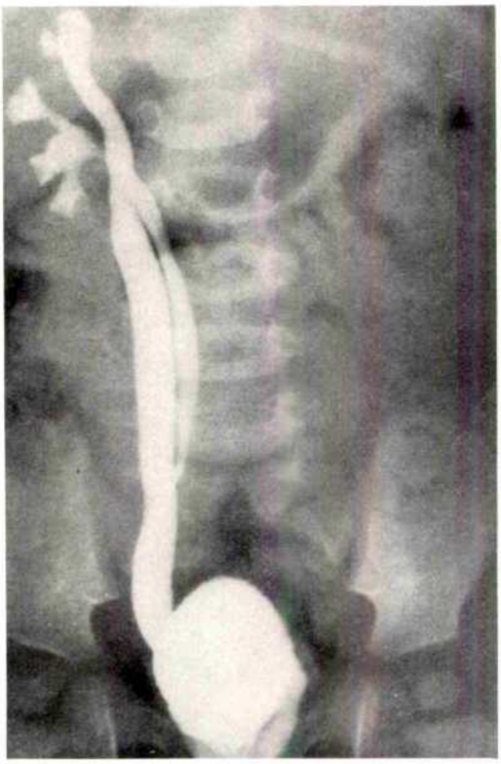


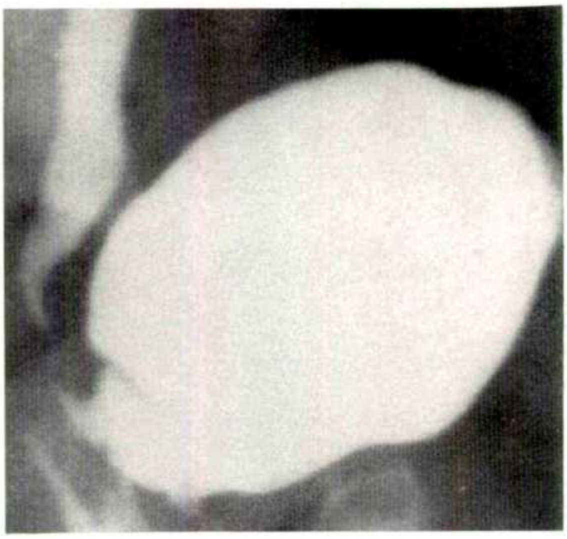
FIG. 21

Fig. 20.—Micturating cystogram in a boy with severe bladder outflow obstruction. A prolapsed ectopic ureterocele has produced a cone-shaped dilatation of the posterior urethra and the ureterocele itself shows as a faint filling defect.

Fig. 21.—Diagrammatic view of ruptured ectopic ureterocele.



A



B

FIG. 22

A and B, Cystogram in a girl with right duplex kidney and ruptured ectopic ureterocele. Reflux occurs into both ureters and the characteristic deformity of ruptured ectopic ureterocele is shown in the base of the bladder.

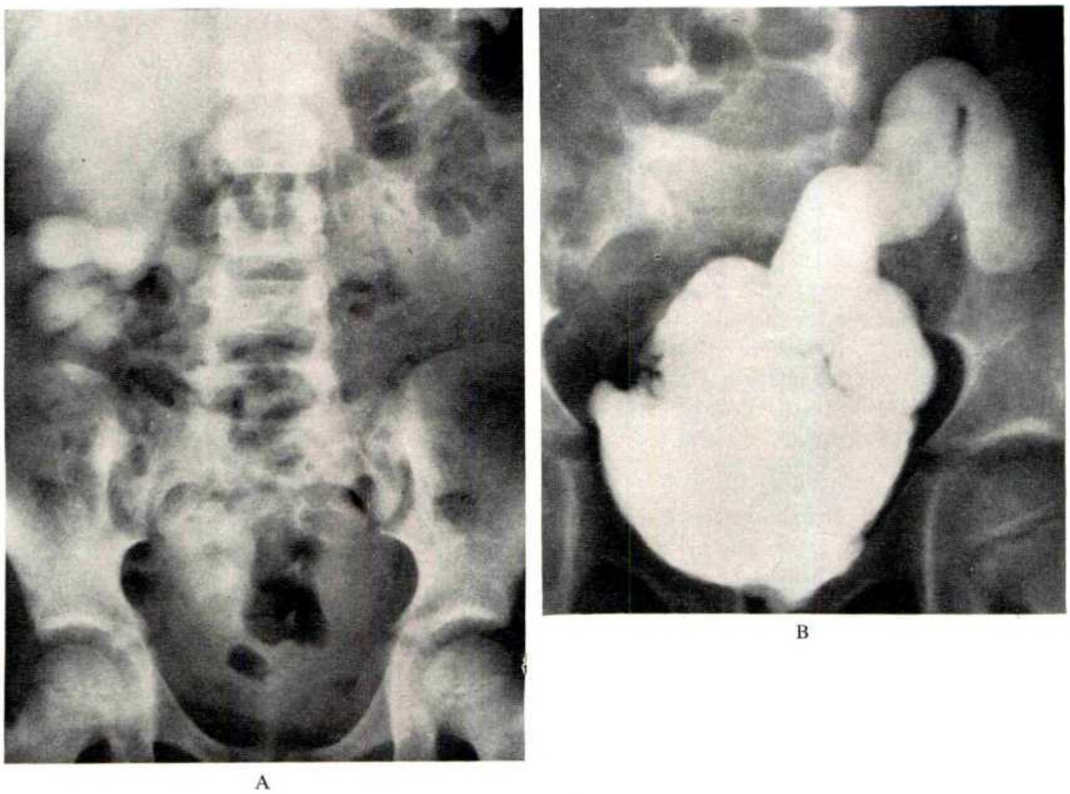


FIG. 23

A, I.V.P. in a boy with gross bilateral hydronephrosis and no opacification on the left. B, Cystogram shows a grossly hypertrophied bladder with reflux into left lower pole ureter and a characteristic deformity of ruptured ectopic ureterocele at the base of the bladder on the left side.

The films illustrated here are from a series of over 150 cases referred from many hospitals and we would like to acknowledge our thanks to the radiologists concerned, but in particular to the staff of the radiological department at The Hospital for Sick Children and the St Peter's Hospitals.

British Journal of Urology (1972), 44, 434-450

TREATMENT OF BLADDER CARCINOMA BY A HYDROSTATIC PRESSURE TECHNIQUE

Report on 43 Cases

By Karl Helmstein

Department of Surgery, Södersjukhuset, Stockholm, Sweden

Since 1966 the author has developed a new method for treatment of cancer of the urinary bladder based on the following considerations:

Increased intravesical pressure induces a reduction of blood circulation and thus anoxia of the bladder wall. Certain findings indicate that tumour tissue is particularly vulnerable, while the normal bladder mucosa is more resistant.

Hydrostatic pressure treatment of the bladder is technically easy and can be regarded as non-dangerous. Its repeated use is possible if unsatisfactory results are obtained or if recurrence takes place.

Technique of Hydrostatic Pressure Treatment.—1. *Anæsthesia.*—Total atony of the bladder wall is induced by high epidural anæsthesia. Inadequate anæsthesia increases the risk of muscle rupture in the bladder wall. It is important that additional doses of the anæsthetic should be given at the first signs of pain or discomfort. The moderate fall of blood pressure sometimes observed during high epidural anæsthesia is of advantage, as a lower intravesical pressure may

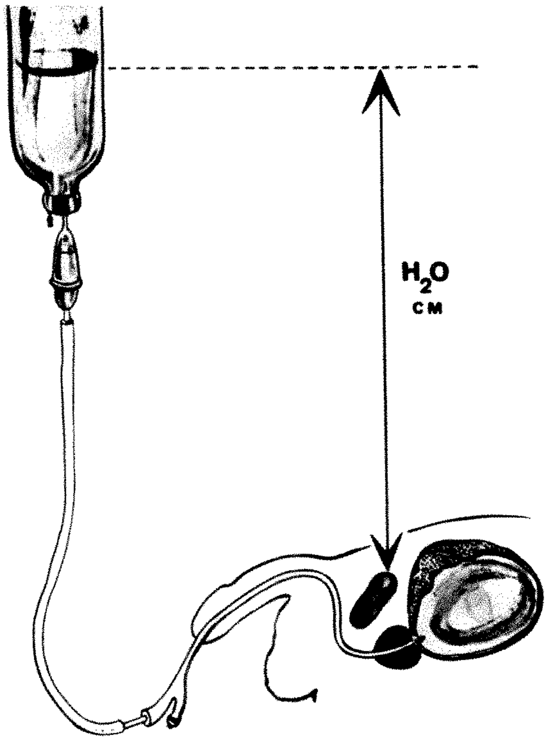
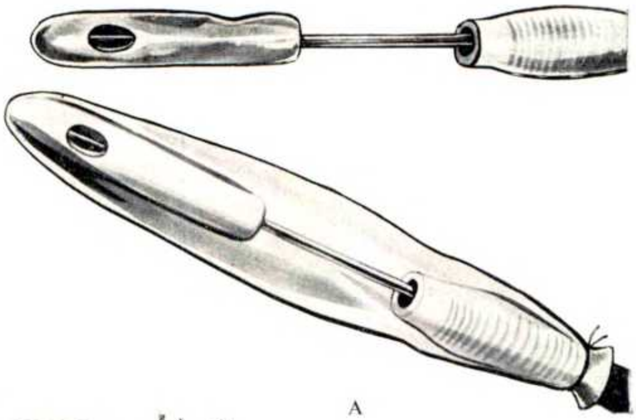
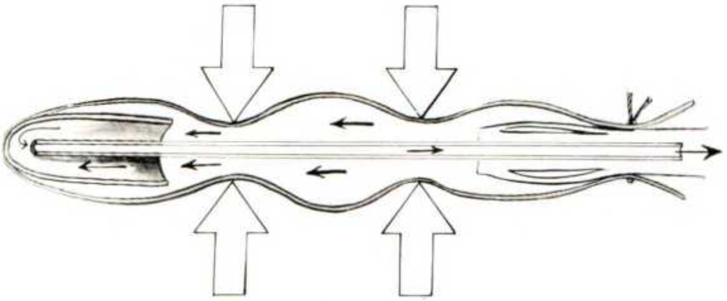
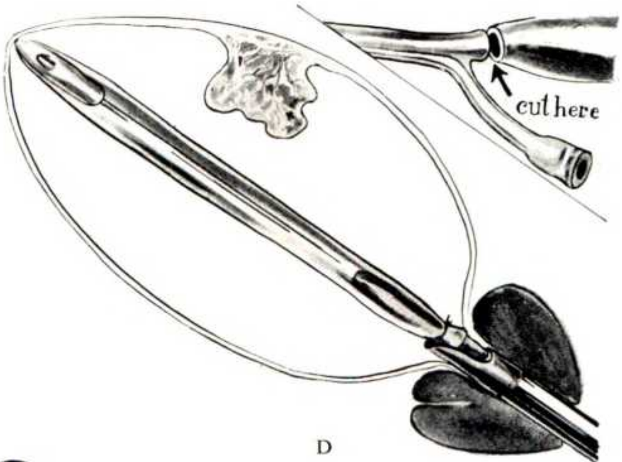


Fig. 1
Technical arrangements for hydrostatic pressure treatment.

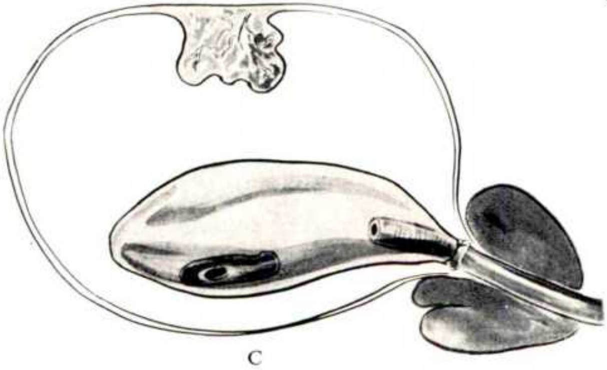
FIG. 2


A


B



D


C

Technique of hydrostatic pressure treatment—balloon method. The following equipment is used:
28 Ch Resectoscope, 16 Ch Foley catheter, 1·2 mm. steel tube of 40 cm. length, round and medium sized balloon.

A, The catheter is totally divided just below its tip, and the steel tube is threaded through. The tip is reinforced by the introduction of an internal steel sleeve. The balloon is now drawn over and fastened just behind catheter's own balloon. Advancing the steel tube will now draw the balloon out to a long, fine rubber tube, which can easily pass through the resectoscope. The free catheter tip will act as a buffer to prevent perforation of the balloon. B, Sometimes an air-bubble may form in the balloon. The air can be expelled through the steel tube by manual compression of the balloon before its introduction through the resectoscope. C, The resectoscope is now withdrawn by 5-6 cm. Care should be taken not to dislodge the balloon. The steel tube is thereafter removed and the balloon is filled with 100 ml. of fluid, instilled in 20 ml. portions. The fluid should enter without resistance and correct location of the balloon is checked by rectal palpation (exclude dislodgement into urethra). The large mouthpiece of the Foley catheter is cut off so that the resectoscope can be completely withdrawn, leaving the catheter and the balloon *in situ*. The balloon of the Foley catheter is now filled with fluid to avoid dislodgement of the large balloon into the urethra (of particular importance in female patients). D, Thereafter the large balloon is filled with fluid using an infusion set with saline. To overcome the elasticity of the balloon a pressure exceeding the required intravesical pressure by 25 cm. H_2O is used. Rapid increase of the drip rate during the procedure indicates imminent risk of bladder rupture (see Complications).

then be effective. Sometimes a more pronounced blood pressure fall may occur, probably induced by severe stretching of the bladder. This complication can normally be controlled by conventional measures.

2. *Hydrostatic Pressure Treatment.*—Two different types of intravesical infusion technique have been used to increase the intravesical pressure to a level close to the diastolic blood pressure. Both techniques have been used in about the same number of treatments:

(*a*) Using a *Foley catheter* the bladder is filled with saline. The increased intravesical pressure presses the balloon of the catheter against the internal meatus and escape of fluid is prevented. The required volume of saline varies, but is generally about 1,000 ml. Intravesical pressure can easily be adjusted by variation of the elevation of the infusion set above the patient. When the drip rate slows, an intravesical pressure (in cm. H_2O) has been achieved corresponding to the vertical distance (in cm.) between the infusion set and the patient. At the beginning of the procedure a pressure of 70 cm. H_2O is induced. When this pressure has been reached the infusion set may be raised by 5 cm. at a time. Equilibrium should be awaited before each adjustment, until the intravesical pressure is close to the patient's diastolic pressure. As a rule a final pressure of 100 cm. H_2O (approximately 75 mm. Hg) should not be exceeded. An intermittent drip rate of 30-50/min. may also be seen after complete filling of the bladder, due to further stretching of the bladder wall. A rapid increase of the drip rate to about 100 drops/min. indicates imminent risk of bladder rupture. Complete bladder rupture can be prevented by reduction of the hydrostatic pressure or discontinuance of the treatment.

(*b*) The second technique consists of the introduction of a large *rubber balloon* into the bladder. The procedure is illustrated and described in Figures 2, A-D. The pressure required to overcome the elasticity of the balloon amounts to about 25 cm. H_2O. The true intravesical pressure upon the bladder mucosa is thus represented by the elevation of the infusion set in cm. minus 25 cm. An elevation of 125 cm., equivalent to a pressure of 75 mm. Hg, should not be exceeded. Again with this technique a rapid increase of the drip rate indicates imminent risk of bladder rupture.

When using the Foley catheter method, leakage of saline may occur if the balloon is not fitting tightly within the bladder neck. This may either be due to surface irregularities of the balloon, which should be checked before use, or of the bladder neck, *e.g.*, due to prostate hypertrophy. The leakage can usually be controlled by slight tension on the catheter and by adjustment of the filling of the balloon.

The residual volume of saline in the bladder after treatment may differ considerably from the instilled volume during treatment (in 2 cases, 1000 ml., in 2 others 700 ml. and in 4 cases 200 ml.), even when leakage has not occurred. A possible explanation may be retrograde filling of the ureters. As, however, clinical symptoms have not been observed, it is more likely that saline diffuses through small perforations in the bladder wall.

Another explanation may be the loss of luminal membrane in neoplastic epithelia, as reported by Hicks *et al.* (1971), resulting in increased perfusion of fluid through such areas.

These difficulties can be eliminated by use of the balloon method which, however, has other disadvantages. Certain areas of the bladder wall, *e.g.*, areas inside a diverticulum or behind the trigone (especially in cases of prostate hypertrophy) may be more or less protected from the pressure effect. In other cases a small tumour can be situated in the shadow of a large one, and thus be protected from the pressure effect. If during treatment a fluid layer is maintained between the bladder wall and the balloon, fluid is pressed into the diverticula and other irregularities resulting in constant pressure all over the bladder wall.

Increased intravesical pressure is maintained for 5½-7 hours and thereafter an indwelling catheter is kept in place for a few days to 1 week.

Material.—During the last 5 years we have treated a total of 70 patients. The results from 43 patients who have been controlled for a prolonged period of time are reported. The youngest

TABLE I

Age and Sex Distribution of Material

Sex	Age Groups					Total
	≦49	50-59	60-69	70-79	≧80	
Female . .	...	2	2	6	2	12
Male . .	2	6	9	11	3	31
Total .	2	8	11	17	5	43

TABLE II

Tumour Stages and Malignancy Grades (IUAC-classification according to Bergkvist *et al.*, 1965) as well as Gross Pathology of the Material

Stage and Malignancy	Gross Pathology	Number of Patients
T_4 M_{IV}	Solid	4
T_4 M_{III}	Solid	4
T_3 M_{IV}	Solid	1
T_3 M_{III}	Solid	8
T_2 M_{III}	Solid	4
T_2 M_{II}	7 single papillary tumours, 1 multiple papillomatous tumour	8
T_1 M_{II}	5 single papillary tumours, 9 multiple papillomatous tumours	14
	Total	43

TABLE III

Tumour Size and Malignancy Grades of the Material

Malignancy Grade	Greatest Diameter of Tumour in cm.				Total No. of Patients
	2-5	5-7	7-15	Multiple Papillomatous ½-2	
II	10	1	1	10	22
III-IV	4	11	6	...	21
Total	14	12	7	10	43

patient was a man of 26 and 22 patients were over 70 years old. The age and sex distribution is given in Table I.

IUAC classification, malignancy rating after Bergkvist *et al.* (1965), as well as the gross pathology of the tumours are summarised in Table II.

Thus, the material includes 21 highly advanced malignant tumours (M III-IV) and 10 patients with multiple papillomata. Cases of grade I malignancy have not been treated.

Tumour size and malignancy grades are given in Table III.

In 5 patients the duration of the disease exceeded 2 years, in 8 cases the duration was 1-2 years, in 23 patients 3-11 months and in 7 cases 1-2 months.

In the 43 patients 58 hydrostatic pressure procedures were carried out. For reasons explained below 15 treatments in 8 patients were excluded from this report:

On 6 occasions hydrostatic pressure treatment was carried out in patients suffering from *perivesical growths* (5 patients: 3 cases T_4M_{IV} and 2 cases T_4M_{III}). In such conditions a palliative effect only can be expected. In spite of widespread necrosis total destruction could not be achieved. Four of the patients died 2 months after treatment and 1 patient, treated twice, died 14 months after the first treatment—all deaths were due to tumour growth. These cases are not further discussed.

In 3 cases early in the series *bladder perforation* occurred and treatment was discontinued. These cases are also excluded.

Six procedures in 5 patients were excluded because of a rapidly *increasing drip rate* or *anæsthetic failure*. All 5 patients were re-treated within 1 week and these latter procedures are included in the material.

Thus 43 procedures carried out in 35 patients are available for final evaluation. Three patients each were treated twice, and 2 patients each 3 times because of recurrences or unsatisfactory effect of the first procedure.

RESULTS

The treatment result was classified as total necrosis if viable tumour cells could not be found, either at biopsy, resection, or in patients who succumbed at post-mortem examination, or if cystoscopy showed an intact normal epithelium. If necrosis included parts of the tumour only, the treatment result was classified as partial necrosis. After hydrostatic pressure treatment total necrosis was observed in 27 of the 35 patients and partial necrosis in 8.

1. **Total Tumour Necrosis.**—(*a*) *Hydrostatic Pressure Treatment Only.*—In 23 patients total tumour necrosis was obtained after hydrostatic pressure treatment only (Table IV). In 4 of these patients previous pressure treatment had resulted in partial necrosis only (these cases are also included in Table VI). In 2 of these patients total necrosis was obtained after one subsequent pressure treatment. In 1 of them resection was performed after the first pressure treatment and recurrence occurred within 14 months after resection.

One patient suffering from multiple papillomata had to be re-treated twice before total tumour necrosis was obtained. Another patient had a recurrence after the first pressure treatment and had to be re-treated before total necrosis was obtained.

In 3 of the 23 patients cystotomy was carried out subsequent to pressure treatment. A transmural biopsy from the tumour area was made through the bladder wall. One patient showed total tumour necrosis 1 week after treatment. The second patient had developed granulation tissue after demarcation of the tumour. In the third patient the tumour had disappeared 5 weeks after treatment.

(*b*) *Hydrostatic Pressure Treatment Followed by Other Measures.*—This group includes 4 patients. In 3 patients resection and reimplantation of the ureter was carried out 4, 5 and 7 weeks after pressure treatment. The resected areas showed total necrosis of the tumour without trace of tumour cells. One patient was treated by radiotherapy although no tumour rest was found at cystoscopy.

Twelve patients (Tables IV and V) comprise the most malignant group (T_4M_{IV}-T_2M_{III}). Eight of these 12 patients are alive: 2 patients 3½ years after their first pressure treatment, 3 patients about 2 years and 3 patients approximately 1 year.

TABLE IV

Description of 23 Patients with Total Tumour Necrosis after Hydrostatic Pressure Treatment Only
Patients 18, 34, 9, 37 also included in Table VI

Case	Age	Sex	Stage Malig-nancy	Pathological Type	Greatest Diameter cm.	Duration of Disease (Months or Years)	Survival (Months)	Recurrence (Months)	Dead		Notes
									No Cancer (Months)	Of Cancer (Months)	
43 EH	76	M	T_4M_{IV}	Solid	7-15	1 y. ?	..	..	1 m	..	Perf. ulcer + uræmia
5 SK	73	F	T_4M_{III}	Solid	5-7	1 m.	46	..	..	..	Cystotomy
32 TE	72	F	T_3M_{IV}	Solid	5-7	6 m.	26	..	..	..	
15 OS	64	M	T_3M_{III}	Solid	5-7	1 m.	42	..	..	..	Cystotomy
21 GL	73	M	T_3M_{III}	Solid	5-7	4 m.	..	..	24 m.	..	Cystotomy. Treated for wide-spread skin cancer before treatment of bladder cancer. Died with skin cancer
33 GF	68	M	T_3M_{III}	Solid	5-7	3 m.	26	..	..	..	
39 GE	54	M	T_3M_{III}	Solid	5-7	6 m.	21	..	..	..	
18 BN	57	M	T_2M_{III}	Solid	..	28 m.	19	14	..	..	Earlier pressure treatment without total necrosis. Re-section and recurrence. One more pressure treatment with total necrosis (not included) (see also Table VI)
30 MP	76	F	T_2M_{III}	Solid	..	1 m.	27	8 + 21	..	..	Re-treated twice with total necrosis (not included)
34 NK	51	M	T_2M_{III}	Solid	..	3 m.	22	18	..	..	Treated earlier without total necrosis. Re-treated once with total necrosis (not included) (see Table VI)
16 YJ	55	M	T_2M_{II}	Papillary	2-5	5 y.	41	..	..	..	
28 HF	80	F	T_2M_{II}	Papillary	5-7	3 m.	..	..	10 m.	..	Suicide
35 EF	85	M	T_1M_{II}	Papillary	2-5	4 m.	25	..	..	..	
41 JH	65	M	T_1M_{II}	Papillary	2-5	2 m.	20	..	..	..	
3 AN	80	M	T_1M_{II}	Papillomatosis	2½	3 y.	..	..	10 m.	..	Arteriosclerosis
9 KD	55	F	T_1M_{II}	Papillomatosis	2½	5 y.	44	5	..	..	Treated 3 times, once without total necrosis. Repeated electrocoagulation and 2 more pressure treatments with total necrosis (not included) (see Table VI)
20 FK	72	M	T_1M_{II}	Papillomatosis	2½	2 m.	35	..	..	..	
26 TJ	73	M	T_1M_{II}	Papillomatosis	2½	2 y.	30	9	..	..	The recurrence treated by repeated electrocoagulations
29 GP	64	M	T_1M_{II}	Papillomatosis	2	2 y.	28	8	..	..	The recurrence treated by repeated electrocoagulations. One more pressure treatment, with total necrosis (not included)
36 EJ	77	M	T_1M_{II}	Papillomatosis	2½	2 y.	24	12	..	..	The recurrence treated by electrocoagulations
37 ChM	26	M	T_1M_{II}	Papillomatosis	2½	1 y.	21	8	..	..	Treated earlier twice without total necrosis. Two more pressure treatments with total necrosis (not included) (see Table VI)
40 GA	70	F	T_1M_{II}	Papillomatosis	2½	14 y.	20	13	..	..	One pressure treatment with partial necrosis and electro-coagulation (not included)
42 JJ	62	F	T_1M_{II}	Papillomatosis	2	2 m. ?	20	12	..	..	Electrocoagulation

TABLE V

Description of 4 Patients with Total Tumour Necrosis after Hydrostatic Pressure Treatment followed by other Measures

Case	Age	Sex	Stage Malig-nancy	Pathological Type	Greatest Diameter cm.	Duration of Disease (Months) or Years)	Survival (Months)	Recurrence (Months)	Dead		Notes
									No Cancer (Months)	Of Cancer (Months)	
27 KL	70	M	T_3M_{IV}	Solid	7-15	6 m.	. .	. .	2	. .	Resection. Heart disease
23 IM	55	F	T_2M_{III}	Solid	2-5	10 m.	. .	. .	14	. .	Radiotherapy. Sepsis
19 OO	76	M	T_2M_{II}	Papillary	7-15	6 m.	. .	. .	2	. .	Resection. Died from complications after surgery
17 PN	66	M	T_2M_{II}	Papillary	5-7	2 y.	38	35	. .	. .	Resection. Pressure treatment with total necrosis (not included)

TABLE VI

Description of 12 Patients with Partial Tumour Necrosis after Hydrostatic Pressure Treatment
Patients 18, 34, 9, 37 also included in Table IV

Case	Age	Sex	Stage Malig-nancy	Pathological Type	Greatest Diameter cm.	Duration of Disease (Months or Years)	Survival (Months)	Recurrence (Months)	Dead		Notes
									No Cancer (Months)	Of Cancer (Months)	
2 HS	75	F	T_3M_{III}	Solid	5-7	10 m.	. .	42	. .	44	Resection. Cerebral thrombosis
10 SR	59	M	T_3M_{III}	Solid	5-7	4 m.	. .	. .	6	. .	Resection. Peritonitis
18 BN	57	M	T_2M_{III}	Solid	2-5	1 y.	35	14	. .	. .	Resection. Pressure re-treated (see also Table IV)
34 NK	51	M	T_2M_{III}	Solid	2-5	3 m.	25	3	. .	. .	Pressure re-treated (see also Table IV)
14 NB	64	M	T_2M_{II}	Papillary	2-5	3 m.	51	10	. .	. .	Resection. Recurrence—electrocoagulated
24 EN	67	M	T_2M_{II}	Papillary	2-5	2 y.	. .	. .	. .	. .	
24 EN	. .	. .	. .	. .	. .	. .	. .	. .	6	. .	Resection. No recurrence. Heart disease
31 WE	67	M	T_2M_{II}	Papillary	2-5	9 m.	26	. .	. .	. .	Resection
4 LA	45	M	T_1M_{II}	Papillary	2-5	3 m.	45	. .	. .	. .	Subsequent. Electrocoagulation
23 GS	78	M	T_1M_{II}	Papillary	2-5	10 m.	. .	. .	. .	28	Subsequent. Electrocoagulation. Developed another bladder tumour T_2M_{III}, pressure treated (not included). Pneumonia and recurrence
13 AS	71	M	T_2M_{II}	Papillomatosis	2½	15 y.	. .	3	16	. .	Resected and electrocoagulated. Heart disease
13 AS	. .	. .	. .	. .	. .	. .	. .	1	. .	. .	
9 KD	55	F	T_1M_{II}	Papillomatosis	2	5 y.	39	. .	. .	. .	Electrocoagulation (see also Table IV)
37 ChM	26	M	T_1M_{II}	Papillomatosis	2½	1 y.	33	. .	. .	. .	
37 ChM	. .	. .	. .	. .	. .	. .	31	. .	. .	. .	Pressure re-treated (see also Table IV)

One of these patients had recurrences after 8 and 21 months. Two patients had recurrences after 14 and 18 months respectively. These 3 patients were re-treated and remain free from cancer 19, 21 and 27 months after their first pressure treatment. These repeated pressure treatments are not included in the tables.

Four patients from this group died, 2 within less than 2 months, 1 (treated by radiotherapy) after 14 months and another after 24 months. None of them showed signs of bladder cancer at autopsy.

Four of the 6 patients in the group T_2M_{II}-T_1M_{II} are alive, 3 of them without recurrence (1 after approximately 3½ years and 2 after about 2 years). The fourth patient had a recurrence which was re-treated and remains free from cancer 38 months after his first pressure treatment. Two patients from this group died, 1 committed suicide 10 months after pressure treatment and the other died 2 months after treatment, from heart disease. Signs of cancer were not observed at autopsy.

Eight of the 9 patients suffering from multiple papillomata are alive, 1 of them without recurrence 35 months after pressure treatment. Seven patients developed recurrences within 8-13 months. They were either re-treated by pressure treatment or by electrocoagulation. At the last cystoscopic control in May/June 1971, these patients were well (*i.e.*, 1 patient 4 years and 6 patients 2-2½ years after pressure treatment).

One patient died 10 months after pressure treatment; signs of bladder tumour were not found at autopsy.

To summarise: 7 of the 27 patients in whom total necrosis of the tumours had been achieved, died, but none of cancer. Eight of 18 patients with solitary tumours were free from recurrence 2-3½ years following treatment. Three patients with recurrences of highly malignant tumours were re-treated with good effect (follow-up 19, 21 and 27 months respectively). The possibility of repeating pressure treatment without ill effect is one of the advantages of the method.

The results in cases suffering from multiple papillomata seem to be less favourable. On the other hand it has to be remembered that it is also very difficult to treat such patients, with the bladder full of multiple papillomata, by conventional methods. Papillomata have a pronounced tendency to develop recurrences also after a perfect electrocoagulation.

2. **Partial Tumour Necrosis.**—Partial necrosis of the tumour subsequent to hydrostatic pressure treatment was obtained in 12 patients (Table VI). In 4 of these patients total tumour necrosis was obtained by repeated hydrostatic pressure treatment. These patients (Cases 9 KD, 18 BN, 34 NK and 37 ChM) are included in Table IV, and discussed as total necrosis cases.

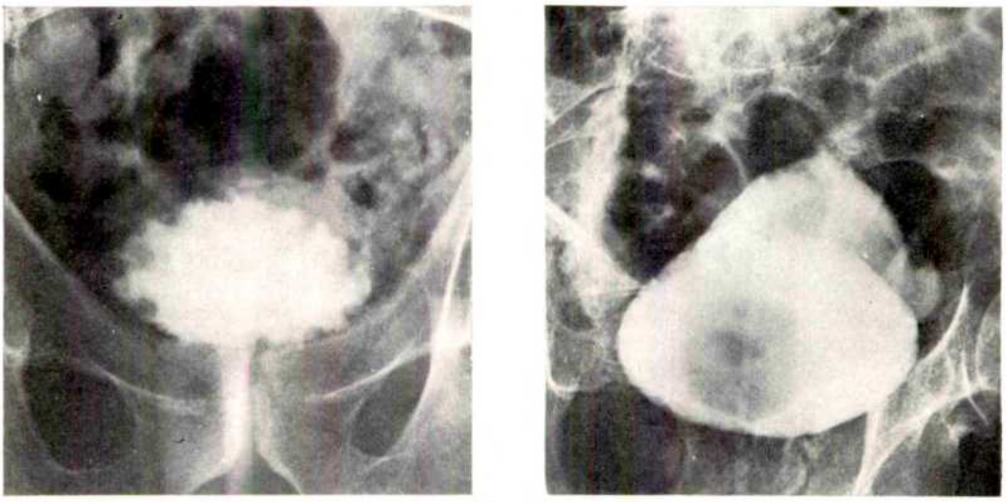
Thus partial necrosis *only* was obtained in 8 patients. Three of these patients were subsequently treated by electrocoagulation. The remaining 5 patients were operated on and in all of them a major part of the tumour was found to be necrotic at resection. In 3 of these 5 patients operation was carried out as soon as 1 week after pressure treatment. The possible development of late necrosis (see below) in these cases cannot be assessed on this account.

The 2 patients in the classification group T_3M_{III}, both resected, died; one of cancer 44 months after treatment but the other after 6 months without evidence of cancer at autopsy.

Three of the 5 patients in the classification groups T_2M_{II} and T_1M_{II} are alive. Two of them were free from recurrences, one 45 months after pressure treatment and electrocoagulation, and the other 26 months after pressure treatment and resection. One resected patient developed a recurrence after 10 months but remains alive 51 months after treatment.

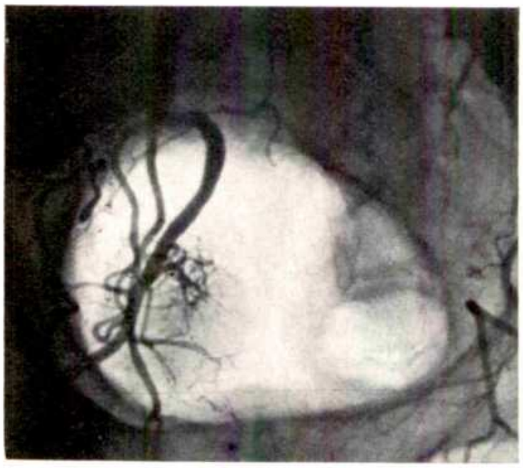
Two patients from this group died, one of them from heart disease without signs of cancer at post-mortem examination. The other patient developed a new tumour (T_2M_{III}) near the bladder neck, which was pressure treated with good effect (not included in this series). The patient died 28 months later of pneumonia; at autopsy, recurrence of the new tumour was found.

Finally, the patient suffering from multiple papillomata, in whom partial necrosis only had been achieved, died 16 months after pressure treatment from heart disease.

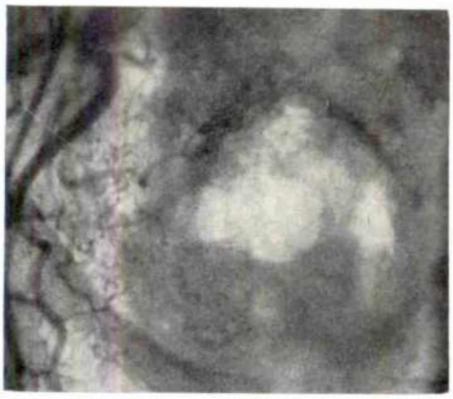


A FIG. 3 B

Patient A. N. (Case 3). Multiple papillomata. X-ray before (Fig. 3, A) and 9 months after pressure treatment (Fig. 3, B).



A

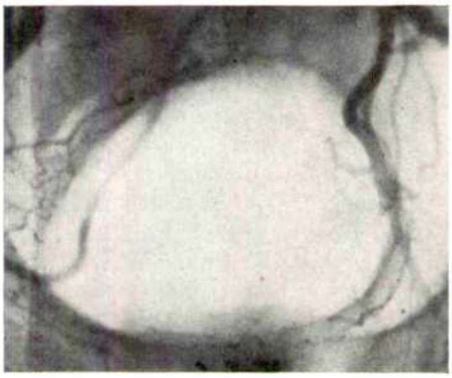


B

FIG. 4

Patient G. F. (Case 33). Solid bladder tumour.

A, 16th May 1969. Before treatment. Pelvic angiography late arterial-capillary phase. Right-sided, round bladder tumour, diameter 3 cm., irregular vessels and moderate tumour stain. No peripelvic invasion. X-ray malignancy III. B, 22nd July 1969. Seven weeks after treatment. Same phase as Fig. 4, A. Incomplete CO_2-filling of bladder. Tumour still visible, but delineation not so distinct as in Fig. 4, A. Thickened bladder wall, moderate tumour stain. C, 2nd February 1971. One year 8½ months after treatment. Late arterial-capillary phase. Normal angiography, no signs of tumour recurrence.



C

3. **X-ray Findings.**—The X-ray findings from 3 patients before and after pressure treatment are reviewed.

Patient A. N. (Case 3) had suffered from multiple papillomata (T_1M_{II}) for 3 years when pressure treatment was carried out. Total necrosis was achieved after 1 treatment. The patient died 10 months after his pressure treatment; signs of bladder tumour were not found at autopsy (Fig. 3).

Patient G. F. (Case 33) suffered from a solid bladder tumour (T_3M_{III}) which was detected 3 months before pressure treatment. Total tumour necrosis was obtained after pressure treatment and the patient was alive 26 months after treatment without recurrence (Fig. 4).,

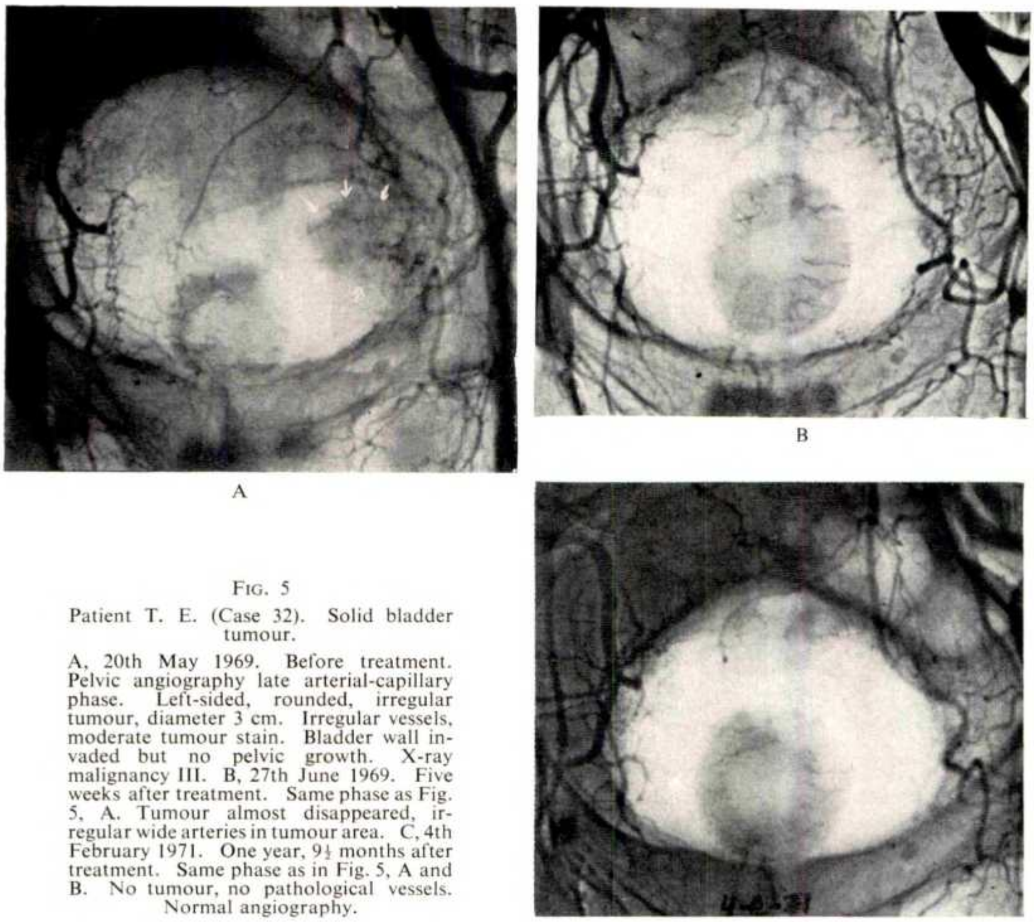


FIG. 5

Patient T. E. (Case 32). Solid bladder tumour.

A, 20th May 1969. Before treatment. Pelvic angiography late arterial-capillary phase. Left-sided, rounded, irregular tumour, diameter 3 cm. Irregular vessels, moderate tumour stain. Bladder wall invaded but no pelvic growth. X-ray malignancy III. B, 27th June 1969. Five weeks after treatment. Same phase as Fig. 5, A. Tumour almost disappeared, irregular wide arteries in tumour area. C, 4th February 1971. One year, 9½ months after treatment. Same phase as in Fig. 5, A and B. No tumour, no pathological vessels. Normal angiography.

Patient T. E. (Case 32) suffered from a solid bladder tumour (T_3M_{IV}) with symptoms for about 6 months before pressure treatment. In this case also total tumour necrosis was achieved by 1 pressure treatment. The patient was alive and well 26 months after pressure treatment, without signs of recurrence (Fig. 5).

4. **Factors of Influence for the Therapeutic Response.**—After the above general evaluation of the treatment results it may be of interest to analyse to what extent various factors may have influenced the therapeutic response to hydrostatic pressure treatment.

TABLE VII

Incidence of Total and Partial Tumour Necrosis respectively—related to Malignancy Grades

Malignancy Grade	Number of Treatments	Necrosis	
		Total	Partial
M II	27	16	11
M III-IV	16	12	4
Total	43	28	15

TABLE VIII

Incidence of Total and Partial Tumour Necrosis respectively—related to the Localization of the Tumour in the Bladder

Localisation	Number of Treatments	Necrosis	
		Total	Partial
Bladder neck . .	7	7	0
Post trigonal . .	5	4	1
Laterally post osteal .	14	6	8
Fundus . . .	3	2	1
Total . . .	29[1]	19	10

[1] Fourteen treatments of multiple papillomata are excluded.

TABLE IX

Incidence of Total and Partial Tumour Necrosis respectively—related to the Duration of Hydrostatic Pressure Treatment

Duration of Pressure Treatment (Hours)	Number of Treatments	Necrosis	
		Total	Partial
<4	4	2	2
4-5	9	3	6
5-6	30	23	7
Total	43	28	15

(*a*) *Degree of Malignancy.*—The incidence of total and partial necrosis respectively was calculated separately for low (M_{II}) and high (M_{III}-$_{IV}$) malignant tumours. The figures discussed in the following refer to the *number of pressure procedures* (43) carried out in the 35 patients described previously.

From Table VII it can be seen that the ratio total : partial necrosis amounts to 16 : 11 in the group of low malignant tumours. The corresponding figures in the high malignant group was 12 : 4, indicating that the latter group reacted more readily to pressure treatment and subsequent anoxia.

(*b*) *Site of the Tumour.*—The incidence of total and partial necrosis respectively, after breakdown of the material in regard to the tumour site, is given in Table VIII. It was evidently more difficult to obtain total necrosis in tumours situated postero-lateral to the ureteric orifices, the ratio total : partial necrosis being 6 : 8, as compared to the ratio for the other areas 13 total : 2 partial. This difference might be explained by the fact that the superior and inferior vesical arteries are situated near the orifices. Thus the lateral part of the trigone is well vascularised and it is more difficult to influence the circulation in this area by pressure treatment.

TABLE X

Incidence of Total and Partial Tumour Necrosis respectively—related to the Duration of Intravesical Pressure at or close to the Diastolic Level

Duration of Intravesical Pressure at Diastolic Level (Hours)	Number of Treatments	Necrosis	
		Total	Partial
<2	11	0	11
2-4	11	8	3
4-6	21	20	1
Total	43	28	15

TABLE XI

Incidence of Early and Late Total Tumour Necrosis as well as Partial Necrosis respectively—related to Malignancy Grades

Malignancy Grade	Number of Treatments	Necrosis		
		Early Total	Late Total	Partial
II	27	13	3	11[1]
III-IV	16	4	8	4[2]
Total	43	17	11	15

Resection one week after pressure treatment. Possible development of late necrosis could not be assessed: [1] 1 case; [2] 2 cases.

(*c*) *Duration of Procedure and Optimal Intravesical Pressure.*—The total duration of hydrostatic pressure treatment as related to the incidence of total and partial necrosis respectively is given in Table IX. Thirteen of 39 procedures lasting for more than 4 hours, failed to result in total necrosis of the tumours. In 7 of these partial failures the procedure had been prolonged for 5-6 hours. On the other hand in 2 of 4 procedures total necrosis was obtained with a treatment duration of less than 4 hours. In both instances, however, the intravesical pressure exceeded the patient's own systolic blood pressure for about half an hour.

The periods of time during which an optimal intravesical pressure, *i.e.*, close to the diastolic blood pressure of the patient, was maintained and the incidence of total and partial tumour necrosis are summarised in Table X.

Still better correlation was found between the time during which optimal intravesical pressure was maintained and the ratio total : partial tumour necrosis.

5. **Incidence of Early and Late Necrosis.**—In the beginning of our series we controlled the patients for 1 week after pressure treatment and thereafter weekly for 6 weeks. We found that necrosis in technically satisfactory procedures started earlier than in technically less satisfactory ones.

In addition the interesting observation was made that the less malignant types of cancer normally showed optimal necrosis, even at the first control examination, *i.e.*, after 1 week. Necrosis in high malignant cancer types was however often less rapid. Four to 5 weeks after treatment necrosis was most often fully developed and significant changes of the local conditions were subsequently not observed.

In Table XI the incidence of early total necrosis, late total necrosis, and partial necrosis is given, as related to the malignancy grades of the tumours. The ratio early : late total necrosis was virtually reversed in the 2 groups, with a higher incidence of late necrosis in the more malignant tumours.

COMPLICATIONS

Bladder rupture is the only significant complication observed in connection with hydrostatic pressure treatment. Partial rupture can easily be recognised by an increase of the drip rate. We differentiate between two different types of partial bladder ruptures:

Mucosal hernia, *i.e.*, millimetre-sized gaps between the muscle fibres. This type was mainly observed after pressure treatment using the Foley catheter method.

Larger ruptures of the musculature with intact mucosa, which may occur when the balloon method is used.

By decrease of the intravesical pressure or discontinuance of the procedure total rupture can always be prevented.

In the first 13 treatments we observed 2 total ruptures and 1 perforation through an ulceration in the tumour area. In retrospect it may be said that in these cases far too high intravesical pressure had been induced. In 1 of the cases transfer of the patient to another room may have been a contributing factor. Logically, all abrupt moves with the patient should be avoided during pressure treatment. All patients healed without complications after subsequent treatment on conventional lines. Partial ruptures were observed in 5 patients. Cystoscopy showed mucosal rupture only in 2 cases. In 1 case microscopic examination of the resected area showed partial rupture of the muscle layer. In another 2 cases a characteristic, rapid increase of the drip rate was observed and they may also be regarded as having developed subtotal perforations. The patients were treated with an indwelling catheter and remained free from further complications.

Bleeding complications were not a problem. We have only seen one moderate hæmorrhage, which stopped after rinsing with Epsilon amino-capronic acid.

This low incidence of hæmorrhage is of interest considering the alleged higher risk of hæmorrhage in connection with increased intravesical pressure. The following possible explanations are given:

During pressure treatment the intravesical pressure is significantly higher than the increase in pressure induced by pathological processes.

The bladder urine contains quite significant amounts of fibrinolytic enzymes such as urokinase. These enzymes may have an unfavourable effect on the formation of hæmostatic plugs. During and after pressure treatment the bladder is filled with saline, which cannot be assumed to influence the local hæmostatic mechanisms.

It was also interesting to observe that hæmorrhage existing already before commencing treatment stopped after pressure treatment.

Serious changes in bladder function as a result of pressure treatment were not observed. After pressure treatment an indwelling catheter is kept in place for a few days or a week. Subsequently slight dysuria may persist for a few weeks.

Mortality related to pressure treatment has not occurred in our material.

DISCUSSION

Our results indicate that complete necrosis of tumour tissue in the bladder wall can frequently be achieved by an increase of intravesical pressure for several hours. The normal bladder mucosa on the other hand is less severely affected and will easily regenerate.

In rat experiments Mehrotra (1953) showed that the circulation of the bladder wall began to decrease when the intravesical pressure reached 100 cm. water, *i.e.*, 75 mm. Hg. A further increase of the intravesical pressure circulation resulted in total obstruction of the blood flow and oscillatory movements of the blood corpuscles only were found. Our findings indicate that an increase of intravesical pressure approximating to the patient's diastolic blood pressure is sufficient to decrease the blood circulation in the bladder tumour.

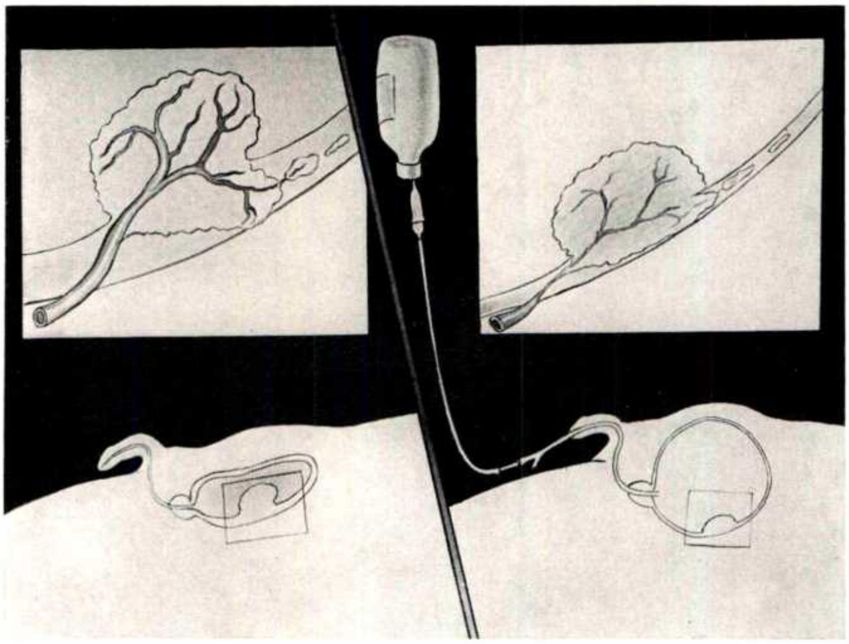


FIG. 6

Localisation and vascularisation of a bladder tumour *with secondaries*. *Upper left:* Conditions under normal intravesical pressure. Circulation also to neoplastic areas in the deeper tissue layers *included secondaries*. *Upper right:* Conditions during hydrostatic pressure treatment. Compression of vessels at the side of their entrance into the bladder wall. Reduced circulation also in deeper tissue layers. *Lower left:* Appearance of a bladder tumour during normal intravesical pressure. *Lower right:* Compression of a bladder tumour during hydrostatic pressure treatment.

Selective necrosis limited to the neoplastic regions may have different explanations:

The abnormal vessels in the terminal vascular bed of the tumour may collapse more easily when intravesical pressure is increased. The vessels supplying the tumour with blood enter always through the bladder wall (Fig. 6). When the bladder is stretched hard during the procedure these vessels may be compressed thus explaining the necrosis observed in the deeper parts of the tumours. These circumstances may also have an effect on metastases in the deeper tissue layers, *e.g.*, in the lymphatic vessels. Moreover, because of their changed metabolic pattern tumour cells may be more sensitive to anoxia than cells in the normal bladder mucosa.

In this context it is interesting to note that none of the reported cases had secondaries at autopsy, irrespective of whether total or partial necrosis had been achieved.

In a number of patients necrosis was observed comparatively late after hydrostatic pressure treatment. This was more often seen after treatment of histologically highly malignant tumours than of less malignant types (Table XI).

Certain observations indicate that these late reactions may be due to immunological processes.

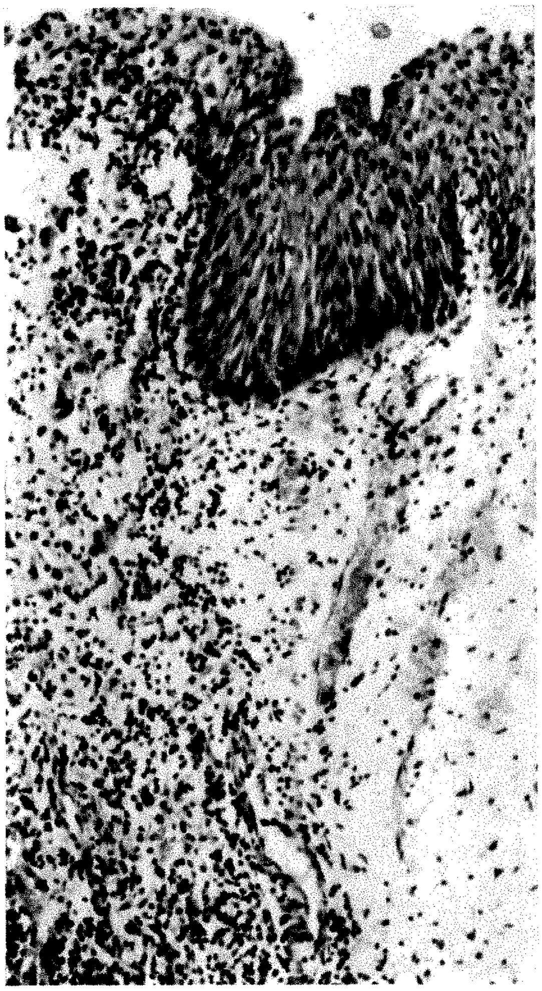


FIG. 7

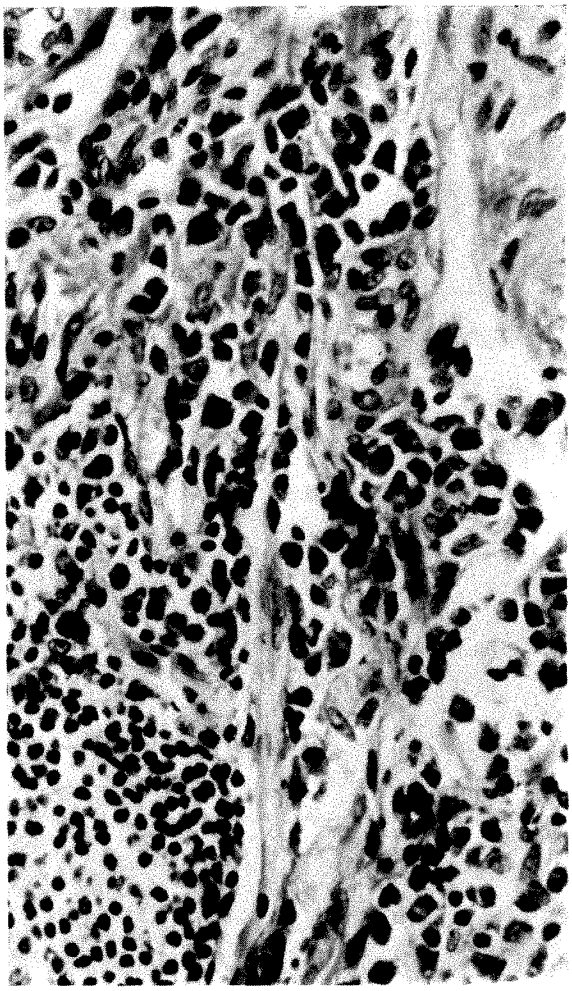


FIG. 8

Fig. 7.—Patient N. K. (Case 34). Bladder mucosa 5 weeks after hydrostatic pressure treatment. Plasma-lymphocytic infiltration in degenerated cancer tissue only. Photo micrograph. × 160.

Fig. 8.—Patient N. K. (Case 34). Bladder carcinoma 5 weeks after hydrostatic pressure treatment. Small remnants of degenerated and disintegrated cancer cells intermingled with numerous plasma cells and lymphocytes. Photo micrograph. × 400.

Professor Perlmann's group from the Wenner-Gren Institute in Stockholm have in preliminary experiments found specific immunological reactions against bladder cancer cells in tissue cultures after hydrostatic pressure treatment. These reactions may be mediated by substances released from cells damaged or destroyed by the hydrostatic pressure treatment (Bubenik *et al.*, 1970*a*, *b*).

Another observation which points in this direction is the finding of late lymphocyte or plasma cell infiltrations in preparations from repeated biopsies after hydrostatic pressure treatment (Figs. 7 and 8). These cells were mainly localised around the remnants of degenerated cells in regions in which necrosis had been induced by hydrostatic pressure treatment (Helmstein and Moberger, 1971).

SUMMARY

The results from our first 43 treatments suggest the following:

High malignant tumours are more sensitive to pressure treatment than low malignant types (Table VII).

The situation of the tumour is of importance in so far as tumours situated close to the passage of larger vessels through the bladder wall responded poorly (Table VIII).

The duration of increased intravesical pressure at values corresponding to or exceeding the diastolic (and below the systolic) blood pressure to a large extent determine the treatment result (Tables IX and X).

Thus we found partial necrosis in 1 patient only who, considering the above-mentioned factors, was treated under optimal conditions, stressing the importance of taking these factors into account when deciding upon the duration of the procedure.

Hydrostatic pressure treatment is a new method and the exact definition of its indications has not yet been finalised. Patients treated up till now fall into the following groups:

Extensive papillomatosis responding poorly to other treatment regimens. Recurrences, mostly isolated tumours, may occur 8-13 months after pressure treatment. These tumours are easily controlled by electrocoagulation treatment.

Large isolated tumours of malignancy grade II in patients not suited for more extensive surgical interventions.

Highly malignant tumours are most sensitive and this type of tumour represents in our opinion the most important indication. This is in particular true for tumours not infrequently seen close to the trigone or bladder neck. Total extirpation of the bladder and urinary diversion are in such cases the only alternative surgical treatment.

Highly malignant, far advanced tumours not accessible for irradiation or surgery. The palliative improvement obtained in such cases is not without importance, considering that some of the patients lived for a further year after treatment not forgetting the influence of the procedure on pain, voiding need, hæmorrhage and urinary incontinence. In addition improved general well-being of the patients is not infrequently seen.

Hydrostatic pressure treatment may be combined with other therapeutic procedures such as irradiation. Irradiation after pressure treatment should however be delayed for 1-2 months in order not to disturb possible immunological processes.

After technical failures of hydrostatic pressure treatment, the procedure may be repeated. Even following mucosal hernia, treatment may be repeated after approximately 1 week. The second treatment, however, should always be carried out by the balloon method.

After muscle ruptures at least 2 months should elapse before re-treatment.

If the primary result is unsatisfactory the interval before re-treatment may depend on the grade of malignancy of the tumour. If total necrosis of the tumour has not been achieved, low grade malignant tumours may be re-treated already after 1 month as necrosis normally then is completed. In highly malignant tumours at least 2-3 months should elapse.

We have no experience regarding pressure treatment of recurrent bladder cancer in previously irradiated patients. If such patients are to be treated, however, it should be remembered that the immunological response of irradiated patients may be decreased. This may have an unfavourable influence upon the result of pressure treatment.

Pressure treatment after previous electrocoagulation presented no difficulties. The same is true for patients having undergone bladder surgery, due to other diseases.

Finally, the balloon-method is technically less difficult than the Foley catheter technique. It is therefore recommended that the balloon method should be used initially until experience in the application of the hydrostatic pressure treatment has been gained.

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PATHOLOGY AND PROGNOSIS FOLLOWING TOTAL CYSTECTOMY FOR CARCINOMA OF BLADDER

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The course of malignant tumours depends not only on the efficacy of treatment but also on the aggressiveness of the neoplasm and probably on host resistance. The relation between survival and tumour differentiation, mitotic activity and extent of spread is well recognised, and more recently a correlation has been established between lymphocyte and plasma cell infiltration and prognosis in tumours of the breast and gastro-intestinal tract (Black *et al.*, 1955, 1956; Hawley and Morson, 1970) and between tissue mast cells and prognosis in carcinoma of the cervix (*Lancet*, 1966).

The present study was undertaken to determine the extent to which the pathological features of bladder carcinomas in cystectomy specimens could be related to the subsequent clinical course.

Material and Methods.—The material consisted of total cystectomy specimens from patients under the care of one surgeon (Mr D. M. Wallace) between 1949 and 1967. Most of the operations were carried out at this hospital and the patients were also treated with various forms of radiotherapy. All the available pathological material was reviewed. Tumour type, pattern, pleomorphism, mitotic activity and extent of invasion were assessed in the routine hæmatoxylin and eosin stained sections. Tumour type and pattern were noted according to the Institute of Urology classification (Dukes, 1959), pleomorphism and mitotic activity of tumour cells were assessed on a rough quantitative scale 0-3, and depth of infiltration recorded by anatomical levels so that the findings could be simply translated into either the U.I.C.C. or U.S.A. (Jewett) classification. Elastic Van Giesen stained preparations were used to assess vascular changes and fibrosis in and around the tumour. Alcian blue/Unna Pappenheim stained slides were examined in addition to the hæmatoxylin and eosin preparations to determine the density of plasma cell and tissue mast cell infiltration.

RESULTS

Suitable pathological material was available from 128 patients who survived the immediate post-operative month, and whose present clinical status or ultimate fate was known. Twelve (10 per cent) were alive and well more than 5 years post-operatively, the longest survival time being 16 years, and a further 11 alive and well between 3 and 5 years after operation. Overall 3 and 5-year survival rates were 38 and 23 per cent respectively. As might be anticipated in this age group, a number of the deaths were from unrelated causes, but 49 per cent of patients had died of either local or disseminated bladder carcinoma within 3 years of cystectomy, 42 (33 per cent) in the first post-operative year. Although the 5 year survival rate was 23 per cent, 9 of these 27 patients died of urothelial carcinoma subsequently. In 5 of these, urethral tumours had developed up to 5 years after cystectomy.

Relation between Depth of Invasion and Survival (Table I).—As anticipated, depth of invasion was related to subsequent course, the 5-year survival rate falling from 77 per cent for patients with non-invasive tumours to 2 per cent (1 case) for those with infiltration into the perivesical fat. None of the 10 cases with carcinomatous invasion of prostate lived more than

2 years after cystectomy and 70 per cent of these were dead within 1 year. The greatest difference appeared between the groups showing no evidence of invasion and in which early invasion was present (77 per cent compared with 27 per cent 5-year survival) and between those with deep muscle and perivascular fat involvement (29 per cent compared with 2 per cent 5-year survival). Fifty-seven per cent of patients with tumour infiltrating into perivesical fat died of carcinoma within 1 year of cystectomy and a total of 86 per cent had done so by the end of the third post-operative year. The corresponding figures for cases with the tumour apparently still confined to deep muscle were 29 per cent and 50 per cent respectively.

TABLE I

Relation between Depth of Infiltration of Tumour and subsequent Course

Infiltration	Tumour Deaths in		3-Year Survival	5-Year Survival	Patients still Alive (Years after Cystectomy)	
	1st Year	1st 3 Years			Over 5	3-5
None . . .	1 (5%)	2 (9%)	18 (88%)	13 (77%)	4/17	5/22
Mucosal . . .	1 (7%)	5 (33%)	6 (40%)	4 (27%)	3/15	0/15
Superficial muscle .	3 (14%)	9 (41%)	11 (50%)	3 (15%)	1/20	2/22
Deep muscle . .	7 (29%)	12 (50%)	9 (38%)	6 (29%)	4/21	3/24
Perivesical fat . .	24 (57%)	36 (86%)	5 (12%)	1 (2%)	0/42	1/42
Prostate and adjacent organs . . .	7 (70%)	10 (100%)	0	0	0/10	0/10

Relation of Tumour Type to Survival (Table II).—Almost all the tumours sectioned were transitional cell or undifferentiated carcinomas. Two patients had squamous carcinomas and both were dead within 2 years of cystectomy. One patient with adenocarcinoma is still alive and well 13 years post-operatively. The transitional cell (differentiated) tumours were divided into apparently pure papillary, mixed papillary and solid, and apparently pure solid types. Most (29 out of 32) of the purely papillary tumours had not invaded into deep muscle, while deep muscle or perivesical fat infiltration was present in 46 of the 59 cases with pure solid or undifferentiated tumours. As expected, pure papillary growths were associated with the best prognosis, only 9 per cent of patients dying of tumour in the first 3 years after cystectomy and

TABLE II

Relation between Histological Tumour Type and subsequent Course

Type	Tumour Deaths in		3-Year Survival	5-Year Survival	Patients still Alive (Years after Cystectomy)	
	1st Year	1st 3 Years			Over 5	3-5
Differentiated papillary	3 (9%)	6 (19%)	19 (59%)	13 (48%)	3/27	5/32
Differentiated papillary and solid. . .	8 (34%)	17 (50%)	13 (38%)	6 (18%)	4/33	1/34
Differentiated solid .	9 (50%)	13 (72%)	5 (28%)	2 (12%)	2/16	2/18
Undifferentiated . .	21 (51%)	31 (71%)	10 (24%)	5 (13%)	5/38	3/41

48 per cent surviving 5 years or longer. The prognosis for solid transitional and undifferentiated tumours was very similar, with 72 and 71 per cent respectively dying of tumour in the 3 years after cystectomy and only 12 per cent and 13 per cent 5-year survivors. Mixed papillary and transitional cell tumours apparently had an intermediate prognosis.

Relation between Morphological Indicators of Malignancy and Survival.—(A). *Pleomorphism.* —There were too few cases whose tumours showed only slight pleomorphism for satisfactory comparison with the 74 where pleomorphism was marked. Thirty of the latter had tumours infiltrating the perivesical fat and, as might be anticipated, a majority (28) of these failed to survive the third post-operative year. Among the remaining patients with more superficial tumours there were 21 tumour deaths in the first 3 years but 10 patients survived more than 5 years after cystectomy, indicating that marked pleomorphism is not necessarily associated with a poor prognosis. This finding was not unexpected since most patients in this series had been treated pre-operatively with radiotherapy and the epithelial response was often still evident at the time of cystectomy.

(B). *Mitotic Activity.*—It is generally accepted that the number of mitoses, in most tumours, is an indication of their aggressiveness; this was confirmed in the present study (Table III) the 3 and 5-year survival rates for patients with tumours showing only slight mitotic activity and those with marked (two or more mitoses per high-power field) mitotic activity were 60 and 46 per cent compared with 26 and 12 per cent respectively. Compared with the group showing slight mitotic activity, deaths from tumour in the first 3 years after cystectomy were almost twice as high in patients with highly active tumours and the proportion of patients with such tumours who were still alive and well more than 5 years post-operatively was less than half of the former group. This finding also applied for the superficially infiltrating (*i.e.* not beyond superficial muscle) tumours alone, 3-year deaths for carcinoma being more than twice as frequent (40 per cent compared with 17 per cent) in cases with high tumour mitotic activity and the 5-year survival rate about half (12 per cent compared with 25 per cent). It was not possible to make a similar comparison of the cases with deeply invasive tumours since only 9 in this group showed low mitotic activity.

TABLE III

Relation between Mitotic Activity and subsequent Course

Activity	Tumour Deaths in		3-Year Survival	5-Year Survival	Patients still Alive (Years after Cystectomy)	
	1st Year	1st 3 Years			Over 5	3-5
Low	6 (22%)	9 (33%)	16 (60%)	11 (46%)	4/24	3/27
High	32 (40%)	50 (63%)	21 (26%)	9 (12%)	5/75	5/80

Permeation of Lymphatics by Tumour and Survival (Table IV).—Permeation of lympathics was also associated with a worse prognosis, the 3 and 5-year survival rates for patients with and without lymphatic vessel invasion being 18 and 12 per cent compared with 52 and 32 per cent respectively. Seventy-eight per cent of patients with tumour in the vesical lymphatics died of their tumour within 3 years of cystectomy and almost half died in the first year, approximately twice the rate of patients without demonstrable lymphatic invasion. The difference between the presence and absence of lymphatic infiltration was also demonstrable when superficial and deeply infiltrating (into and beyond deep muscle) tumours were considered separately. Lymphatic infiltration could only be demonstrated in 9 patients with superficially infiltrating tumours but 4 of these patients (44 per cent) had died of tumour by the end of their third post-operative year compared with 12 (25 per cent) of 48 whose lymphatics appeared free of tumour at the time of cystectomy. With deeply infiltrating tumours the difference was less well marked (83 per cent, compared with 59 per cent). It must, however, be remembered that underdiagnosis of lymphatic permeation is likely in this study, since only two or three blocks of tumour were available for review in most cases.

TABLE IV
Influence of Carcinomatous Permeation of Lymphatics on Survival

	Tumour Deaths in		3-Year Survival	5-Year Survival	Patients still Alive (Years after Cystectomy)	
	1st Year	1st 3 Years			Over 5	3-5
Present	24 (48%)	39 (78%)	10 (18%)	6 (12%)	5/50	1/51
Absent	18 (24%)	28 (37%)	39 (52%)	21 (32%)	7/65	10/75

Relation between Blood Vessel Infiltration and Survival.—The number of specimens with tumour in vascular channels was small, 16. In all except 2 tumour extended into the perivesical fat. Only one of these patients survived more than 5 years after cystectomy, but rather surprisingly the proportion dying of tumour in the first and first 3 post-operative years was approximately the same as in those without vascular invasion (44 and 69 per cent respectively compared with 40 and 64 per cent). Again limited sampling may partly explain this unexpected finding.

Single versus Multiple Tumours.—Comparison of the fate of the 41 patients with a single bladder tumour and the 79 with multiple tumours shows no important difference. The 3 and 5-year survival rates were 34 and 22 per cent compared with 43 and 26 per cent respectively and deaths due to carcinoma in the first 3 post-operative years were 56 and 49 per cent.

Relation of Pattern of Infiltration and Survival.—Most of the infiltrating tumours showed an " en bloc " type of spread, *i.e.*, the advancing border being composed of relatively large coherent, well-defined masses of tumour cells, but amongst deeply invasive tumours almost a half (29 out of 74) showed a diffuse infiltration with poorly defined small groups and single tumour cells forming the outer border. In contrast to previous observations (Mostofi, 1968) survival was not related to the type of " edge " in the present series. Five-year survival rate was identical (15 per cent) for both groups, 3-year survival similar (28 per cent for " en bloc " invasion and 33 per cent for the diffuse pattern) and deaths from tumour within 3 years of cystectomy were 66 and 65 per cent.

Involvement of Other Urothelium.—(A). *Urethra.*—Sections of urethra were available in 46 cases. The presence of malignant change in the urethra epithelium at the time of cystectomy was not associated with a lower survival rate, the 3 and 5-year figures were 37 and 21 per cent respectively compared with 43 and 9 per cent for patients without apparent urethral tumour. However, subsequent development of urethral carcinoma carried a bad prognosis. Eight patients developed a urethral recurrent tumour up to 5 years following cystectomy, 4 were invading when excised, and 3 of these patients were dead within 15 months of recurrence becoming apparent.

(B). *Ureter.*—Sections were available in only 39 cases. In 16 the ureteric epithelium also showed carcinomatous changes and 14 (87 per cent) of these patients had died of carcinoma within 3 years of cystectomy compared with 65 per cent of the 23 cases where no ureteric tumour had been seen.

Relation of Lymph Node Metastases to Survival (Table V).—The poor prognosis associated with tumour deposits in regional lymph nodes is well recognised and was confirmed in the present study. In contrast to Whitmore and Marshall's (1962) finding that patients with not more than 2 nodes involved had some chance of a 5-year survival, none of the patients with lymph node deposits in the present series survived 5 years after cystectomy. Sixty per cent died of tumour in the first year and 95 per cent were dead by the end of the third year. The contrasting fate of patients with and without lymph node deposits was apparent in both the superficial and deeply infiltrating tumours. Although only 3 patients with superficially infiltrating tumours had lymph node invasion, all were dead of carcinomatosis within 3 years of cystectomy, compared with only 17 per cent from the 30 cases without lymph node involvement. In the deeply invasive tumours all 17 cases with tumour deposits were dead within 3 years compared with only 50 per cent of the 14 with nodes free from tumour. Unfortunately, no nodes were available for review in a large number of the earlier cases in the series.

TABLE V

Influence of Tumour Deposits in Lymph Nodes on Survival

	Tumour Deaths in		3-Year Survival	5-Year Survival	Patients still Alive (Years after Cystectomy)	
	1st Year	1st 3 Years			Over 5	3-5
Present . . .	12 (60%)	19 (95%)	1 (5%)	0	0/20	0/20
Absent	3 (7%)	19 (43%)	25 (37%)	13 (35%)	8/37	7/44

Cellular Response around the Tumour and Survival.—A correlation between the density of the chronic inflammatory infiltrate around the infiltrating edge and the prognosis has been demonstrated in carcinomas of the gastro-intestinal tract and breast (Black *et al.*, 1955, 1956; Black and Speer, 1958). A rough quantitative estimate of cellular response around the invading edge of the vesical tumours was therefore made on the available material in this study and the survival times compared both for cellular infiltration as a whole and the individual components. Polymorphonuclear cell infiltration was ignored for the purposes of this part of the study. The findings showed that although an absence of cellular response, in particular plasma cell response, was associated with a poor prognosis, a heavy cellular infiltrate did not necessarily indicate a better one.

(A). *Density of Cellular Infiltration around the Invading Edge* (Table VI).—Cases with only slight degrees of cellular infiltration fared worst than those with a marked degree; 3 and 5-year survival rates were 9 and 6 per cent respectively in the first group compared with 49 and 25 per cent in the latter. Eighty-four per cent of those with a poor cellular response had died of tumour within 3 years of cystectomy compared with 43 per cent of those with intense cellular infiltration around the invaded edge. This difference was also apparent when superficial and deeply infiltrating tumours were considered separately. When only a slight degree of cellular infiltration was seen, 3 of the 6 patients with superficially invading lesions and 24 of the 26 with deeply invasive tumours died of their tumour in the first 3 years, while of those showing marked inflammatory cell infiltration, only 3 of the 14 patients with superficial lesions and 14 of those of the 23 with deep ones did so.

TABLE VI

Relation of the Degree of Cellular Infiltration around the Invading Edge of Tumour and Survival

Degree	Tumour Deaths in		3-Year Survival	5-Year Survival	Patients still Alive (Years after Cystectomy)	
	1st Year	1st 3 Years			Over 5	3-5
Slight	16 (50%)	27 (84%)	3 (9%)	2 (6%)	1/31	1/32
Marked . . .	11 (30%)	16 (43%)	18 (49%)	8 (25%)	4/32	5/37

(B). *The Pattern of Cellular Infiltration* (Table VII).—Cellular infiltration around the tumour edge was patchy in most specimens reviewed; only a quarter showed confluent bands of mononuclear cells. Comparison of the survival times for these 2 patterns showed that the confluent pattern was associated with a lower proportion of deaths from tumour (44 per cent in the first 3 years after cystectomy compared with 65 per cent of those with a patchy infiltrate). Three and 5-year survival figures for the 2 groups were 44 and 33 per cent for the former and 24 and 7 per cent for the latter. As with the density of cellular infiltration, the different survival rates for the 2 patterns remained when superficial and deeply invasive tumours were considered separately.

TABLE VII

Relation of Pattern of the Cellular Infiltrate around the Invading Edge of Tumour and Survival

Pattern	Tumour Deaths in		3-Year Survival	5-Year Survival	Patients still Alive (Years after Cystectomy)	
	1st Year	1st 3 Years			Over 5	3-5
Confluent . .	9 (36%)	11 (44%)	11 (44%)	8 (33%)	5/24	1/25
Patchy . . .	28 (38%)	48 (65%)	18 (24%)	5 (7%)	2/69	5/74

(C). *Plasma Cell Response* (Table VIII).—A finding of few plasma cells around the invading tumour edge was associated with a worse prognosis than intense plasma cell response. Three and 5-year survival rates were 20 and 7 per cent in the former group compared with 46 and 20 per cent in the latter and 75 per cent of patients with only slight plasma cell infiltration had died within 3 years of cystectomy. Although the proportion of deaths from tumour was less in cases with dense plasma cell infiltration, nevertheless almost half of this group too had died of carcinomatosis in the 3 years following cystectomy. This relationship between the density of plasma cells and the death rate from the malignant disease was also apparent when superficial and deeply infiltrating tumours were considered separately.

(D). *Lymphocyte Response.*—Survival did not appear related to the intensity of lymphocytic infiltration around the tumour invading edge. Three and 5-year survival figures for the 31 cases with only slight lymphocyte infiltration were 23 and 10 per cent respectively compared with 30 and 11 per cent for the 40 cases with dense lymphocyte infiltration. When the findings for superficial and deeply infiltrating tumours were examined separately, there were too few cases

(5) with only slight lymphocyte infiltration in the superficially invading group for useful comparison but in the deeply invasive tumours where the number of cases in each group was approximately equal (26 and 25) the 5-year survival rates were identical (8 per cent), the 3-year almost so (15 and 16 per cent) and tumour deaths within 3 years of operation also differed by only 1 per cent (81-80 per cent).

TABLE VIII

Relation of the Degree of Plasma-cell Infiltration around the Infiltrating Edge of the Tumour and Survival

Degree	Tumour Deaths in		3-Year Survival	5-Year Survival	Patients still Alive (Years after Cystectomy)	
	1st Year	1st 3 Years			Over 5	3-5
Slight. . . .	19 (43%)	33 (75%)	9 (20%)	3 (7%)	1/42	2/44
Marked . . .	12 (35%)	16 (47%)	15 (44%)	6 (20%)	4/30	4/34

Miscellaneous Observations.—The degree of eosinophil and tissue mast cell infiltration, presence of vascular changes and degree of fibrosis round the tumour were also assessed and no relation with survival was found. Attempts to assess lymph node changes other than tumour deposition (sinus histiocytosis follicular hyperplasia, plasma-cell response) were inconclusive. Relatively few nodes were available for review and a high proportion of these showed loss of architecture and fibrous replacement of the type associated with previous radiotherapy or lymphangiography.

DISCUSSION

The relationship between prognosis in bladder tumours and the depth of infiltration, tumour type and lymphatic invasion is already known (McDonald and Thompson, 1948; Pugh, 1959; Wallace, 1959; Mostofi, 1968; Poole-Wilson and Barnard, 1971). The present study also shows that the prognostic value of these findings is not influenced by radiotherapy. Additional findings of prognostic importance were the degree of mitotic activity and cellular response around the invading tumour. However, the latter did not entirely correspond with experience previously quoted in breast and gastro-intestinal tumours. Absence of cellular (particularly plasma-cell response was associated with a very poor prognosis, but dense peritumour cellular infiltration was not particularly associated with a good prognosis, over half of the cases dying of tumour within 3 years of cystectomy. The high incidence of chronic infection and inflammatory changes associated with bladder tumours seems the most likely explanation of this finding, since histological examination cannot distinguish between cells which appear in response to an inflammatory stimulus and those which may represent an immunological response to tumour.

SUMMARY

The histopathological features of cystectomy specimens of carcinoma of bladder have been reviewed and related to the subsequent clinical course. The cases studied had also had some form of radiotherapy before cystectomy.

Deep invasion, poor differentiation and high mitotic activity in the tumour, lymphatic vessel permeation and lymph node metastases were all associated with a high proportion of deaths from tumour in the first 3 and 5 years following operation, as were absence or patchy distribution of round-cell infiltration around the invading tumour edge, particularly a poor plasma cell

response. No relation was found between the clinical course and degree of pleomorphism of the tumour or fibrosis, vascular changes, lymphocyte, eosinophil or tissue mast-cell infiltration in the tissues surrounding the tumour, or to lymph node histology apart from the presence or absence of actual tumour deposits.

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A PROGNOSTIC INDEX FOR CARCINOMA OF BLADDER BASED ON HISTOPATHOLOGICAL FINDINGS IN CYSTECTOMY MATERIAL

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One of the problems in comparing different methods of treatment for carcinoma of bladder has been the lack of uniformity in pathological reporting. Although some type of classification having a high correlation with prognosis is clearly most desirable, it is clear from the previous study that many pathological characteristics must be considered. Any pathological report which includes tumour type, differentiation, mitotic activity, depth of invasion, lymphatic permeation, type and pattern of cellular response around the tumour and the presence of tumour in lymph nodes must inevitably be long and unwieldly. Condensation of this information into a simplified code would therefore appear advantageous. Neither the U.I.C.C. nor the U.S.A. grading systems take account of all the pathological findings now shown to be related to prognosis and the U.I.C.C. system has the additional disadvantage of not distinguishing between deep muscle and perivesical fat invasion (both are included as P.3) although the prognosis in the latter has been shown to be very much worse (McDonald and Thompson, 1948, and in the present series). An attempt has therefore been made to translate the clinico-pathological correlations previously established into a numerical factor which would indicate prognosis and might also be useful for comparison for different forms of therapy.

The relevant pathological features were given numerical values based on their prognostic implications (see Tables I to VIII) as follows:

Depth of infiltration	None—0
Confined to mucosa Not beyond superficial muscle	1
Not beyond deep muscle	2
Into or beyond perivesical fat	3
Tumour type	
Differentiated papillary	0
Differentiated papillary and solid	1
Differentiated solid Undifferentiated	2
Mitotic activity—marked	1
Lymphatic vessels permeated by tumour	1
Tumour deposit in *lymph nodes*	3
Cellular reaction around invading edge	
Scanty	1
Patchy	1
Confluent	0
Moderate or dense	0
Density of plasma cell infiltration around infiltrating edge	
Scanty	1
Moderate or heavy	0

The figures for each specimen were added together to form a prognostic factor (P.F.). Where more than one tumour was present and the histological characteristics varied, those of the worst tumour were used. The relationship between this prognostic factor and survival was examined in 117 cases, 64 in which all the pathological features had been assessable and 53 in which all except the lymph nodes were available and where the prognostic factor migh ttherefore have been higher if all the pathological material had been available for review. The results show a clear correlation between the prognostic factor and prognosis (Table). For low P.F.s (4 or less) the prognosis was relatively good, 3 and 5-year survival rates were 75 and 65 per cent respectively. Only one of the 36 cases in this group died of tumour within 3 years of cystectomy and 9 (28 per cent) were still alive and well more than 5 years after operation. In the cases with high P.F.s (10 or more) the prognosis was universally poor. All the 26 cases in this group had died of tumour within 3 years of operation, approximately two-thirds (65 per cent) in the first year. In the intermediate group with P.F.s of 5 to 9 inclusive, the prognosis was intermediate. Three and 5-year survival rates were 29 and 14 per cent respectively. Thirty-two of the 55 patients in this group (57 per cent) had died of tumour within 3 years of cystectomy and only 5 (10 per cent) were still alive and well more than 5 years later.

TABLE

Correlation between Prognostic Factor (P.F.), Survival Rate and Deaths from Tumour following Cystectomy

P.F.	Tumour Deaths in		3-Year Survival	5-Year Survival	Patients still Alive (Years after Cystectomy)	
	1st Year	1st 3 Years			Over 5	3-5
0-4	0	1 (3%)	27 (75%)	20 (63%)	9/32	4/36
5-9	20 (37%)	32 (57%)	16 (29%)	7 (14%)	5/51	4/55
Over 10 . . .	17 (65%)	26 (100%)	0 (0%)	0 (0%)	0/26	0/26

CONCLUSION

It seems that a prognostic factor for carcinoma of bladder, derived in this way from pathological data, provides a useful and simple indication of the prognosis following cystectomy. In its present form it can only be applied where the full thickness of bladder is available for examination as well as the regional lymph nodes, but within this limitation the prognostic factor should also be of value for comparison of the results of different forms of therapy.

SUMMARY

The histological findings in cystectomy specimens of carcinoma of the bladder have been converted into a numerical prognostic factor with a possible range from 0-12. Patients with a low prognostic factor did relatively well with 63 per cent 5-year survivals, those with a high P.F. were all dead within 3 years of cystectomy and those with intermediate prognostic factors, between 5 and 9, had an intermediate prognosis.

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RADICAL CYSTECTOMY FOR CARCINOMA OF THE BILHARZIAL BLADDER

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CARCINOMA of the Bilharzial bladder in Egypt presents certain particular features, which have been reported before by several authors; viz., Makar (1955), El Sebai (1961). Most of the cases present in an advanced stage, the tumours are usually of the squamous cell type, and are radio-resistant. Cystectomy with urinary diversion seems to be the logical treatment of such cases. This study covers our experience with 137 consecutive patients treated by radical cystectomy for Bilharzial carcinoma of the bladder. The extent of the radical operation is to remove the bladder with its perivesical fascia, peritoneal covering, the prostate, and seminal vesicles; together with the external and internal iliac lymph nodes. In females, the bladder, urethra, uterus, adnexa and upper half of the vagina with pelvic cellular tissue and the above-mentioned lymph nodes are removed.

Material and Method.—The composition of the group as regards age and sex is present in Table I. The male to female ratio was 3·4 : 1. The average age for males was 46 years, for females 37·5 years, and for the whole series 44 years.

TABLE I

Age and Sex Distribution of 137 Patients treated by Radical Cystectomy

	Age in Years								Total
	25-	30-	35-	40-	45-	50-	55-	60+	
Males . .	3	1	13	38	22	19	4	6	106
Females .	4	2	6	8	4	6	1	...	31
Total .	7	3	19	46	26	25	5	6	137

Surgical Technique.—(A) *In the Male.*—A lower right paramedian incision, extending from 2 inches above the umbilicus to the symphysis pubis is employed. The pelvis and the abdominal cavity are explored. The growth is palpated and the degree of mobility of the bladder is assessed. If it is decided to proceed with the radical operation, the operating table is tilted into a high Trendelenburg position and the intestines packed out of the pelvis. The peritoneal incision is extended postero-laterally on either side, along the lateral border of the external iliac vessels up to the common iliac bifurcation. The vas deferens is divided and ligated near the internal ring. The fascia on the ilio-psoas is incised and dissected medially. It will be found to be continuous with the connective tissue covering the external iliac vessels. The fibro-fascial sheath covering these vessels is stripped medially to remove the perivascular lymphatics and lymph nodes. The vessels are gently retracted laterally, and immediately medial and below the now cleaned external vein, the obturator space is exposed. By working right on the psoas and obturator internus muscles, all the pelvic fascia is stripped medially without difficulty. The obturator neurovascular bundle is included in the stripped mass. The obturator nerve is identified and separated from the vessels, which are divided and ligated as they leave the pelvis through the obturator foramen. The fibro-lymphatic mass is now reflected medially. The internal iliac artery is dissected free and ligated in continuity; the branches of its anterior division are divided and ligated.

The ureter is identified where it crosses the common iliac bifurcation, dissected free for 3-4 cm., then divided and its distal end ligated. At this stage, with the pelvic fascio-visceral mass displaced medially, the anatomical structures on the side wall of the pelvis are seen free of all fascial structures. The same dissection is now repeated on the other side of the pelvis.

The reflection of the peritoneum from the rectum to the seminal vesicles and bladder is then incised. The space between the anterior structures and the rectum is opened by a combination of blunt and sharp dissection. A thick wide fascial band will thus result on either side, connecting the bladder, vesicles and prostate anteriorly to the sides of the rectum posteriorly. (The vesico-prostato-pelvic fascia.) It is divided piecemeal between clamps which are underrun later.

The bladder is now free posteriorly and laterally, and the dissection is then carried anteriorly dividing the median pubo-prostatic ligaments on either side between clamps. A curved clamp is placed on the urethra distal to the prostate, and the specimen is excised. Final hæmostasis is achieved by inserting deep catgut sutures between the edges of the levator ani muscles on either side. No attempt is made to reperitonealise the pelvis. Drainage is achieved by a suprapubic sump tube.

TABLE II

Methods of Urinary Diversion

	No.	%
Rectal bladder . . .	81	59·1
Uretero cutaneous . . .	43	31·4
Uretero colic	11	8·0
Ileal conduit	2	1·5
Total	137	100·0

(B) *In the Female.*—The technique differs only in its posterior phase. The peritoneum at the floor of the pouch of Douglas is incised. The rectum is separated from the vagina by blunt dissection. The vesico-vagino-rectal fascia, including the utero-sacral ligaments, now present as a broad fascial sheet on either side, connecting the bladder and the vagina anteriorly with the rectum posteriorly. It is cut piecemeal between clamps which are underrun by catgut. The vagina is incised 2 inches above the introitus. The posterior aspect of the urethra is thus exposed, which is now clamped, and cut distal to the clamp. The cut edges of the vagina are sutured around a sump drainage tube.

The different methods used for urinary diversion are given in Table II.

RESULTS

(A) *Mortality and Morbidity.*—Twenty patients did not leave the hospital alive; an operative mortality rate of 14·6 per cent. The different causes are outlined in Table III.

Twenty-five patients developed 32 post-operative non-fatal complications (Table IV).

TABLE III

Post-operative Mortality

Peritonitis	11
Shock	3
Septicæmia	2
Renal failure	2
Pulmonary embolism	1
Coronary thrombosis	1
Total	20 or 14·6%

TABLE IV

Post-operative Morbidity

Shock		2
Septic complications:	wound sepsis	12
	pelvic collections	5
Chest infection		10
Burst abdomen		3
Total		32

TABLE V

Results of Follow-up

Year Period of follow-up in years	67 3+	68 2+	69 1+	70 −1	Total
No. of cases	42	39	41	15	137
Operative mortality	9	4	6	1	20
Recurrence	9	7	11	5	32
Untraced	4	2	2	0	8

N.B: Operative mortality = 20
Untraced cases = 8
No. of patients followed up = 109

TABLE VI

Onset of Recurrence after Operation in 137 Cases

Onset of Recurrence (Months after Start of Surgery)	Number of Cases	
	No.	%
Less than 3	9	28·1
3-6	12	37·5
6-9	6	18·8
9-12	2	6·2
More than 12	3	9·4
Total	32	...

TABLE VII
Recurrence and Tumour Stage

	P.1	P.2	P.3	P.4	Total
Cases with recurrence .	...	2 (20%)	21 (25·4%)	9 (56·2%)	32
Cases without recurrence .	...	8 (80%)	62 (74·6%)	7 (43·8%)	77
		10	83	16	109

TABLE VIII
Recurrence and Tumour Histology

	Squamous	Transitional	Adenocarcinoma	Total
Cases with recurrence .	19 (26·3%)	11 (35·5%)	2 (33·3%)	32
Cases without recurrence .	53 (73·7%)	20 (64·5%)	4 (66·6%)	77
Total . .	72	31	6	109

TABLE IX
Recurrence and Tumour Grade

	Grade I	Grade II	Grade III	Total
Cases with recurrence .	6 (20%)	11 (25·8%)	15 (41·7%)	32
Cases without recurrence .	24 (80%)	32 (74·2%)	21 (58·3%)	77
Total . . .	30	43	36	109

TABLE X
Recurrence and Lymph Node Involvement

	Positive Lymph Nodes	Negative Lymph Nodes	Total
Cases with recurrence .	9 (56·2%)	23 (24·8%)	32
Cases without recurrence .	7 (43·8%)	70 (75·2%)	77
Total . . .	16	93	109

(B) *Follow up and Recurrence.*—Table V summarises the outcome of this series, as followed up to January 1971.

The time of onset of recurrences as detected clinically after the start of treatment is given in Table VI.

The recurrence rate was retrospectively correlated to four pathological features; viz., the tumour stage (Table VII), the tumour histology (Table VIII), the tumour grade (Table IX) and the lymph node involvement (Table X).

DISCUSSION

The general technical principles employed are similar to those described previously by Paquin and Marshall (1956) and El Sebai (1956). No attempt was made to reperitonealise the pelvis as recommended by Robbins *et al.*, (1949).

The operative mortality of 14·6 per cent compares favourably with other reported figures. Paquin and Marshall (1956) gave a figure of 17 per cent, El Sebai (1962) a figure of 17 per cent, and Whitmore (1962) a figure of 14 per cent. The most important single cause for post-operative mortality and morbidity was septic complications. This can be attributed to the following factors:

1. The length of the operative procedure, with extensive dissection and wide raw area exposed.
2. The necessity of some form of urinary diversion with the attended risk of contamination with infected urine.
3. The mechanical difficulties encountered in proper drainage of the dependent pelvic cavity.

The low incidence of cardiovascular complications in this series can be attributed to the fact that we were dealing with relatively young patients; the average age being 44 years.

Rectal bladder with a terminal left iliac colostomy was the most common method employed for urinary diversion. The technique and the advantages of this procedure were discussed in a previous publication. (Ghoneim, 1970).

Due to the short period of follow-up, the prognosis of this type of cancer, as treated by radical cystectomy, was deduced from correlating the various pathological features of the tumours with the frequency of recurrence, rather than with survival rate. Three factors were found to be statistically significant:

1. The tumour stage.
2. The tumour grade.
3. Positive involvement of the regional lymph nodes.

Since most of the cases (77 per cent) are of the P.3 stage, and since the state of lymph node involvement cannot be clinically assessed, the most important single clinical feature which can influence the prognosis is the tumour grade, a factor which has also been emphasised by Thompson (1960).

More than half of the recurrences occurred within six months of commencement of treatment. Moreover, all the recurrences but two were (localised) in the pelvic cavity. This would suggest that in recurrent cases surgical excision alone was inadequate to deal with the extent of the local pathology. Post-operative irradiation may improve the survival rate, a regime which is now employed in a new series.

SUMMARY

Our experience with 137 consecutive patients with Bilharzial carcinoma of the bladder treated by radical cystectomy, has been outlined.

The surgical technique is described; the post-operative mortality being 14 6 per cent. One hundred and nine patients were followed up for periods between 6 months and 3 years. The incidence of recurrence was found to be statistically related to the tumour stage, grade and positive lymph node involvement. Longer follow-up period is needed for calculation of survival rates. However, from the analysis of these preliminary results, post-operative irradiation is recommended to decrease the incidence of local recurrences.

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ELECTRONIC CONTROL OF INCONTINENCE: A CRITICAL REVIEW OF THE PRESENT SITUATION

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CALDWELL first described a method of controlling incontinence by electronic means in 1965, and used an implanted stimulator designed to achieve contraction of the striated muscles of the pelvic floor. Alexander and Rowan (1968) achieved the same effect by means of an external stimulator taking the form of a standard vaginal ring pessary bearing electrodes activated by a pulse generator. Since that time a number of different devices designed to apply external stimuli have been described, and two features have emerged from the published series. Firstly, the results obtained with the different devices were at variance; secondly, the results published in later series were lower than those published in earlier ones.

The object of this study has been to analyse the results obtained in the combined incontinence clinic of the Institutes of Urology and Obstetrics and Gynæcology in order to assess the effectiveness of electronic devices in the control of incontinence, and to decide whether these devices have a part to play in the management of the clinical problem.

Materials and Methods.—The series consisted of 143 patients, of whom 79 were excluded (Table I). The remaining 64 patients were selected for treatment by electronic means, and the method of investigation of these patients has already been documented (Edwards *et al.*, 1971). Selection was based on the results of two investigations, the cystometrogram, and the urethral pressure profile. Harrison and Paterson (1970) showed that successful treatment by electronic means was less likely in cases with abnormality of the cystometrogram, and 43 patients in the present series were judged to have a sufficiently abnormal cystometrogram to warrant their exclusion from trial of electronic treatment. Nine patients with detrusor dysfunction, 51 patients with sphincter weakness, and 4 patients with a combination of the two problems were included in the trial because an electronic device, as opposed to a mechanical one, gave the greatest pressure profile amplitude increase.

TABLE I

Series Total 143

	Included	Excluded
Sphincter weakness (S.W.)	51	43
Detrusor dysfunction (D.D.)	9	34
Sphincter weakness and detrusor dysfunction (Comb.)	4	2
	64	79

The electronic devices used in this series are shown in Table II. It is not proposed at this stage to enumerate the relative advantages and disadvantages of each device.

TABLE II

First Publications

Device	Reference	Manufacturer
Electronic implant	Caldwell (1965)	Devices Ltd.
Anal plug	Hopkinson and Lightwood (1965)	Cardiac Recorders Ltd.
Electronic pessary	Alexander and Rowan (1968)	Not available commercially[1]
Continator	de Soldenhoff and McDonnell (1969)	Vitalograph Ltd.

[1] Pulse generator for use with pessary made by Devices Ltd.

TABLE III

Overall Results

Type of incontinence	Number	Success	%
S.W.	51	22	43
D.D.	9	4	45
Comb.	4	3	75
	64	29	45

TABLE IV

Results with Different Devices

	Tried in:	Success	%
Vitalograph	16	10	62
Anal plug	7	3	43
Electronic pessary	43	16	37
Implant	2	0	0
Electronic spring device	2	0	0
	70	29	

Results.—*Overall Results.*—Of the 64 patients treated, 29 (45 per cent) reported a satisfactory result. The figures are shown in full in Table III, but the small number of patients presenting with the combined problem makes it unlikely that the high success rate achieved in this group has any particular significance.

Devices Used.—It is shown in Table IV that the highest success rate (62 per cent) was seen with the Vitalograph Continator. It is also seen from this table that 70 devices were tried in all, that is to say that some patients were prescribed a different device when treatment with the first was unsuccessful.

Age.—The largest group was one of 17 patients between 41 and 50 years of age (Table V). In only 7 of these cases was treatment successful. It appeared that the success rate fell as age increased, but we did not consider that age played a major part in influencing the results, and that other factors which will be discussed later were more likely to apply as age increased.

Parity.—This seemed to influence the success rate considerably: of 29 nulliparous patients treated, a successful result was reported in 62 per cent (Table VI); in 35 parous patients the success rate was only 31 per cent.

TABLE V

Age

	Number	Success	%
0–10	6	4	75
–20	1	1	100
–30	5	3	60
–40	6	4	66
–50	17	7	41
–60	15	7	46
–70	5	0	0
70+	9	3	33
	64	29	

TABLE VI

Parity

	Type	Number	Success	%
Nulliparous	S.W. D.D. Comb.	21 6 2	15 2 1	62
Multiparous	S.W. D.D. Comb.	30 3 2	9 1 1	31

Previous Surgery.—Similar results were seen when the effect of previous surgical repairs was assessed; of those patients having had no repairs 60 per cent reported favourably, but only 32 per cent of those who had had previous repairs (Table VII).

Parity and Previous Surgery.—When these two preceeding factors were considered together, the results were even more divergent (Table VIII). The success rate was highest in those patients who had neither had repairs nor borne children, and was as high as 71 per cent. The lowest success rate was encountered in parous patients who had been subjected to surgical repairs, at 31 per cent.

Statistics.—The patients were subdivided into two groups, a group in which treatment had been successful, and a group in which it had been unsuccessful. Patients in the first group tended to be younger than patients in the second, and the difference between the ages of the two groups was significant when analysed by Student's *t*-test ($t = 2{\cdot}48$; $P < 0{\cdot}01$). Patients in the first group were also more likely to have higher control profile amplitudes than those in the second group, and the difference between the control profile amplitudes in the two groups was also statistically significant ($t = 1{\cdot}43$; $P < 0{\cdot}05$). It has been established (Edwards and Malvern, 1971) that the profile amplitude falls with increasing age, and we felt therefore that these statistical differences cancelled each other out. On considering the improvement produced in the urethral pressure profile by electronic stimulation, the increase produced in the profile amplitude was equally and highly significant in each group ($t = 4{\cdot}27$; $P < 0{\cdot}0005$). In other words, the production of an increase in the sphincter resistance, as measured by the urethral pressure profile, although statistically significant, bore no relation to the clinical success of the electronic gadget which produced this significant increase.

TABLE VII

Previous Surgery

	Type	Number	Success	%
None	S.W. D.D. Comb.	23 7 0	15 3 0	60
Previous repairs	S.W. D.D. Comb.	28 2 2	9 0 0	32

TABLE VIII

Parity and Previous Surgery

	Type	Number	Success	%
Neither	S.W. D.D.	16 5	13 2	71
Repairs No children	S.W. D.D. Comb.	5 2 1	2 0 1	37
Children No repairs	S.W. D.D.	7 2	2 1	33
Both	S.W. D.D. Comb.	23 1 2	7 0 1	31
		64	29	

DISCUSSION

The fall in the reported success rates of external electronic control of incontinence is disappointing. Alexander and Rowan reported a single successful case in 1968; Riddle *et al.* (1969)

a 57 per cent success rate; Harrison and Patterson (1970) a 52 per cent success rate and Rowan (1970) a 46 per cent success rate. The success rate in the present series was 45 per cent and we suggest that this level would be the anticipated success rate in any large series. The exception to the rule is the Exeter series, which is maintaining a high success rate of 78 per cent in the treatment of 88 cases of female stress incontinence with electronic implant (Flack, 1971) (Table IX).

The failure to correlate success to an improvement of the sphincter resistance, as measured by the urethral pressure profile, led us to abandon our original working hypothesis that successful electronic treatment was dependent on such an increase. We therefore think it reasonable to suggest that treatment with external electrode-bearing appliances could be undertaken on an entirely random basis, with little alteration in the success rates. As far as treatment with implanted electrodes is concerned, the failure to correlate success to an objective measurement poses major problems, as it would no longer appear to be the case that increases of sphincter resistance can be taken as a reliable indication that patients will benefit from electronic implant treatment. Despite the excellent results produced by Caldwell and his colleagues in Exeter, we consider that there is very little indication for undertaking electronic implant in stress incontinence, however resistant, outside such specialised units.

TABLE IX

Published Records and Success Rates

Date	Author(s)	Device	Number	% Success
1965	Caldwell *et al.*	Implant	1	100
1966	Hopkinson and Lightwood	Anal plug	1	100
1967	Caldwell	Implant	36	66
1967	Hopkinson and Lightwood	Anal plug	9	33
1968	Alexander and Rowan	Electronic pessary	1	100
1968	Alexander and Rowan	Implant	14	64
1968	Alexander and Rowan	Implant	17	59
1968	Caldwell *et al.*	Implant	31	74
1969	Riddle *et al.*	Implant	8	52
1969	Riddle *et al.*	Electronic pessary	9	
1969	Riddle *et al.*	Anal plug	4	
1969	de Soldenhoff and McDowell	Continator	28	23
1970	Alexander and Rowan	Electronic pessary	18	72
1970	Harrison and Patterson	Electronic pessary	21	52
1970	Warrell	Electronic pessary	7	57
1970	Warrell	Implant	5	80
1970	Rowan	Electronic pessary	28	46
1971	Edwards *et al.*	Implant	33	70
1971	Edwards *et al.*	Anal plug	21	71
1971	Edwards *et al.*	Vitalograph	4	100
1971	Edwards *et al.*	Electronic pessary	40	40
1971	Glen and Rowan	Implant	13	92

It would also appear from the results that have been shown that electronic control by external means is likely to succeed in those cases where operation is ideally indicated, and is likely to fail in those cases in which surgery is also likely to fail. It may be that the reason for failure in the cases discussed is the muscle fatigue which most workers in the field of electronic control have shown to take place during prolonged pelvic floor stimulation. Alternatively, it may be that stimulation of the pelvic floor muscle does not correct the basic defect in cases of sphincter weakness.

It would probably be fair to conclude that, in the short term, external electronic treatment might be a very useful method in controlling incontinence in those patients with sphincter weakness who are awaiting admission for surgical repair. As a long-term method of control there is probably little case for electronic treatment except in those cases who do not wish to have an operation, and in those cases in whom an operation is contra-indicated for medical reasons.

SUMMARY

1. The results obtained in a series of 64 patients with incontinence treated by electronic methods are discussed.

2. It is suggested that present methods of predicting success are unsatisfactory, and that treatment might equally satisfactorily be undertaken in a random manner.

3. Electronic treatment is most likely to succeed in those cases where operation is indicated, and is likely to fail in those cases where surgery is also likely to fail.

4. Electronic treatment may provide a useful method of short term control of incontinence, but in the long term it is unlikely to replace conventional methods of treatment.

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AN UNUSUAL COMPLICATION OF THE USE OF BARIUM SULPHATE SUSPENSION IN MICTURATING CYSTOGRAMS

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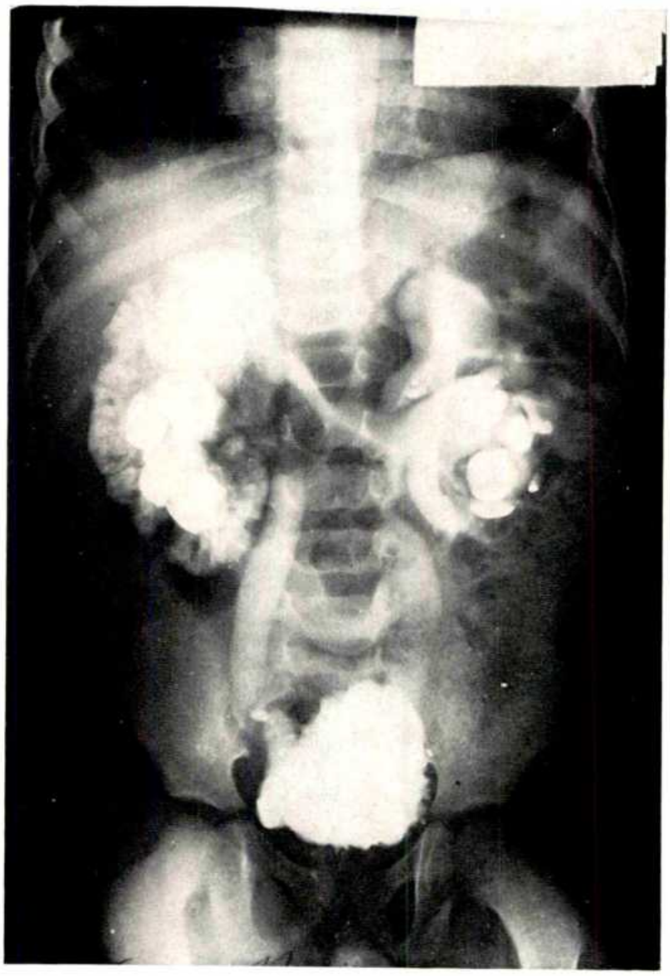
SODIUM iodide solution in a strength of 7-12½ per cent has been used for cystography for many years and is still used in many centres in the developing countries.

Many radiologists consider sodium iodide an irritant solution which may make it difficult to judge ordinary emptying conditions.

In 1952, Kjellberg and associates introduced the use of non-irritating barium sulphate suspension for cysto-urethrography. They claimed improved density and quality of exposure. The use of the barium suspension has been adopted in many centres throughout the world.



One case is here reported showing an unusual complication following the use of barium sulphate suspension for a micturating cystogram in a child.

K. E. M. a 2½-year-old boy attended the Urology Clinic at Korle Bu Hospital, Accra with chronic retention of urine.

An intravenous pyelogram had suggested a possible right vesico- ureteric reflux.

A micturating cystogram was attempted on 15th February 1968 using a barium suspension. The child was not able to void at the time of the examination, but the cystogram obtained is shown in the illustration. There was bilateral vesico-ureteric reflux: on the left the barium suspension went as far as the calcyces. On the right however the barium suspension penetrated the tubules of the kidney as far as the cortex, thus producing a radiographic cast of the kidney.

A plain K.U.B. radiograph taken 1 year later on 31st March 1969 showed the outlining of the tubules of the right kidney with barium unchanged. Unfortunately this later film and the hospital records are missing.

The patient disappeared in between the two examinations and has not attended again since the second examination on 31st March 1969.

DISCUSSION

Kjellberg *et al.*, discussing the use of barium sulphate suspension for cysto-urethrography, state:

" In the beginning of the series we were alarmed by the large refluxes to the ureters and renal pelvis, since we feared complications from retained contrast medium. It was found, however, that the contrast medium which regurgitated into the renal pelvis was usually flushed out rapidly from them. In no case could any remains of it be observed after 48 hours."

Edwards cautions against the use of barium suspensions as a contrast medium for micturating cystograms in the presence of residual urine, bladder diverticula, and vesico-ureteral reflux. He states that the barium residue may act as a nidus for the development of a urinary calculus and he advocates the use of diodone in these circumstances.

This case proves that reflux of barium suspension into the tubules of the kidney is not just a theoretical complication, but a real hazard in the presence of vesico-ureteric reflux.

It would be interesting to know the function of the right kidney as the barium seems to have been permanently deposited in the tubules.

SUMMARY

An unusual complication of reflux of barium sulphate suspension into the tubules of the kidney during cystographic examination is reported.

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British Journal of Urology (1972), **44**, 475-480

AMPHOTERICIN B LAVAGE IN THE TREATMENT OF CANDIDIAL CYSTITIS

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The number of patients with urinary tract candidiasis is increasing in urologic practice. When this fungal disease affects the upper urinary tract, the effects may be dangerous, and the use of intravenous Amphotericin B is indicated (Price *et al.*, 1967).

Several cases of candidiasis, affecting only the urinary bladder, have been described in recent years. Candidial cystitis, while not carrying the same risks as when the kidneys are affected, is usually accompanied by disturbing symptoms resistant to the usual antibiotics, and on several occasions surgical interventions have been performed to evacuate the fungus ball formed.

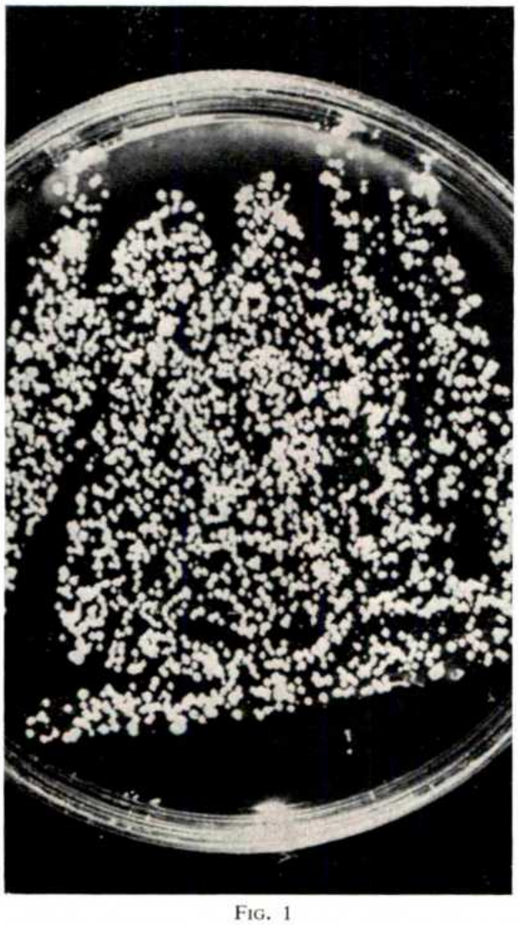

Fig. 1

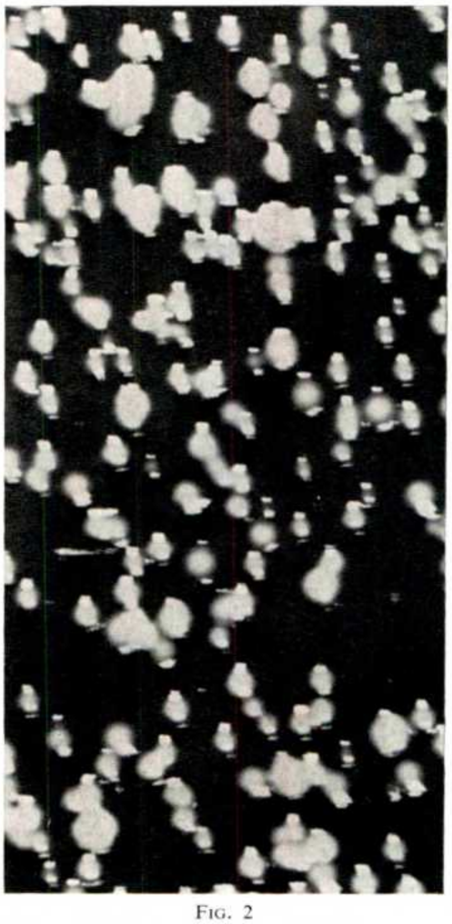

Fig. 2

Fig. 1.—General aspect of Candida albicans, 24-48 hours after inoculation to blood-agar plates.

Fig. 2.—Close-up with typical C. albicans colonies. Note the white, spheric domes, with wet, greasy, brilliant surface.

TABLE I

No.	Patient	Age	Sex	Urologic Disease	Operation	Other Diseases
1	G. R. B. 78.933	70	Male	Prostatic adenoma	Transvesical prostatectomy	...
2	B. M. M. 78.901	68	Male	Prostatic adenoma	Transvesical prostatectomy	Diabetes
3	R. P. M. 79.746	63	Female	Bladder neck hypertrophy	T.U.R.	...
4	M. P. F. 106.942	57	Male	Renal tuberculosis	Nephrectomy	Diabetes, Pulmonary tuberculosis
5	J. B. G. 79.043	75	Male	Prostatic adenoma	Perineal prostatectomy	...
6	O. R. M. 106.517	15	Female	Vesical neurofibromatosis	Cystoscopy	...

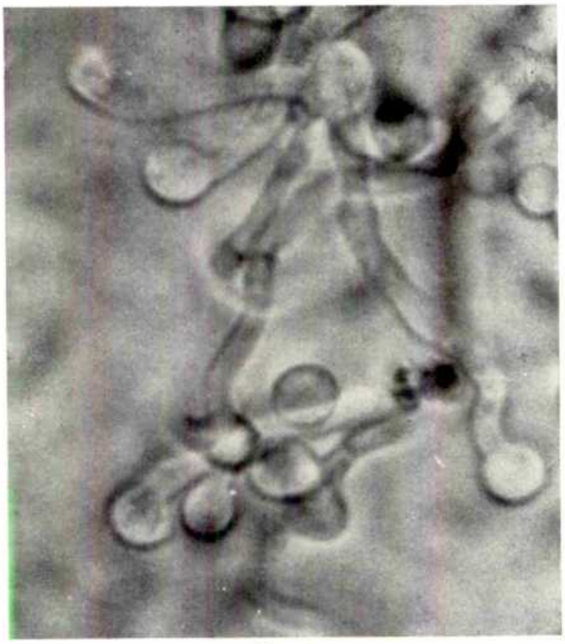

FIG. 3
Production of blastospores.

During the last 6 months, at the Instituto de Urología, the diagnosis of urinary candidiasis has been made in 21 patients. Six of them were treated with Amphotericin B vesical washings, with excellent results and no complications.

Methods.—The urine of all the patients with abnormal urinary sediments was cultured, using plates of blood-agar. The identification of the different species of Candida was made by studying the morphologic characteristics and the various sugar fermentation reactions of each fungus (Figs. 1 and 2).

The 21 patients diagnosed with urinary candidiasis represent 2·6 per cent of all the urine cultures obtained in 6 months. Six of these patients were selected for treatment with Amphotericin B bladder washings. Table I summarises these cases.

The solution was prepared adding 100 mg. of Amphotericin B to 500 ml. of distilled water. Two vesical washings were done daily, using 100 ml. of the solution each time. As most of the patients had already an indwelling catheter, the solution was injected into the bladder, the catheter clamped off and the patient told to hold the solution for a period of 2 or 3 hours, and then empty the bladder. These washings were continued for 6-10 days. Urine culture was done immediately after treatment and several weeks later.

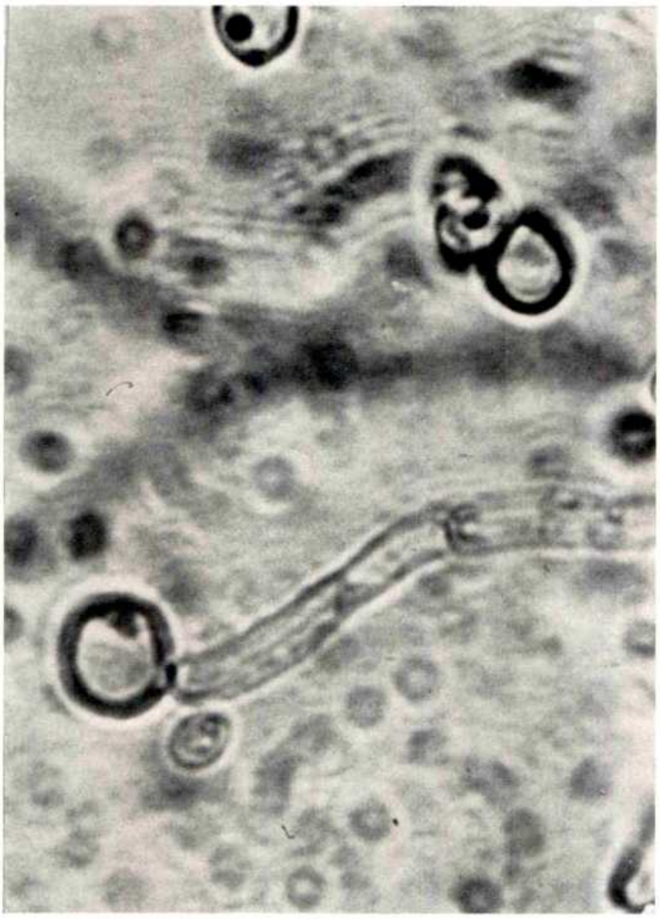

FIG. 4

Production of chlamydospores in corn-meal agar. Note the double cellular wall.

RESULTS

In all cases the Candida disappeared from the urine and the sediment became normal. One case not included in this group, because the washings were done for only 3 days, had persistence of urinary candidiasis for several months. No toxic reaction was seen in any patient and no symptoms of vesical intolerance presented. None of the usual complications of parenteral Amphotericin appeared.

CLINICAL DISCUSSION

The genus Candida belongs to the family Cryptococcacea and class Fungi imperfecti (Blair, 1970). It includes several species: Albicans, Parapsilosis, Stellatoidea, Tropicalis, Krusei, Pseudotropicalis and Guillemondi. Most of them are thought to be pathogenic, but Candida albicans is the most virulent and the only one found in our patients. This fungus is commonly isolated in the mucosæ and frequently cultured from the mouth and fæces of healthy people (Braude, 1962).

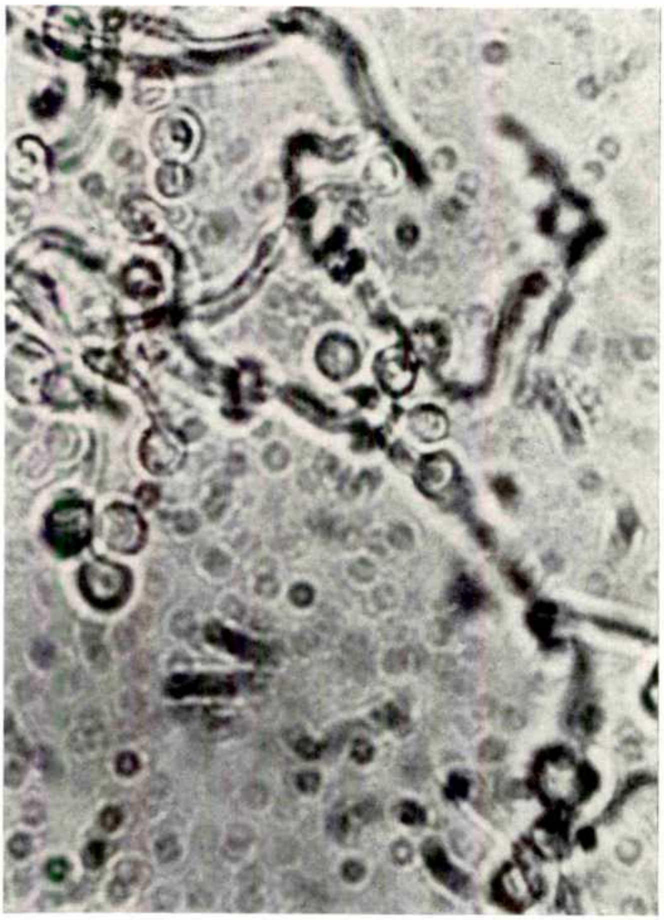

FIG. 5

Microscopic aspect of a fungus ball with blastospores, chlamydospores and leucocytes embedded by mucus.

The incidence of candidiasis has increased during the last 20 years coincidentally with the routine use of broad-spectrum antibiotics (Johnston, 1968). It is thought that the antibiotics kill the saprophytic antagonists of the different types of fungi; this disturbs the ecologic equilibrium and results in the uncontrolled growth of antibiotic-resistant species, like Candida. If this overgrowth takes place in subjects with diminished resistance, like diabetics or cancerous patients treated with antimitotics or radiotherapy, the possibility of developing a mycosis is increased. The urologist is thus faced with patients having catheters or other foreign bodies introduced in the urinary bladder or kidney; these situations undoubtedly favour the establishment of the fungi in the urinary tract.

Candidial cystitis.—Two clinical forms are described:

1. Thrush of the urinary bladder. Moulder (1946) and Sauer (1948) described the appearance of vesical lesions similar to the thrush of the buccal mucosa. They described the presence of whitish, small spots, slightly prominent and adherent to the vesical mucosa. Endoscopic biopsy proved the candidial ætiology.
2. Fungus ball. Fungal conglomerates with leucocytes and mucus may be localised in the pelvis, ureter and bladder (Tennant, 1968) (Fig. 5). Chisholm and Hutch (1961) reported two cases, one of them was a diabetic female with symptoms of cystitis for 3 years and a radiolucent vesical mass; a supra-pubic cystostomy was performed to evacuate a vesical fungus ball. This operation had to be repeated 6 months later because of recurrence of the fungus ball. Rovinescu (1968) has another similar case treated with Pyridium, Chloromycetin and Nystatin, but 1 year later the patient was still eliminating pieces of fungus balls.

The thrush and the fungus ball are advanced forms of candidiasis. Our case 2 showed cystoscopic appearances of vesical thrush and during treatment eliminated true fragments of fungus ball. The remaining cases had symptoms of cystitis with abnormal urinary sediments in which Candida albicans was identified. In our opinion the persistent finding of Candida albicans in the urine is sufficient to establish the diagnosis of urinary candidiasis.

Goldman (1960) thought that at least a minimum of 1,000 colonies per millilitre was necessary to establish pathogenicity but Drouhet has proved the significance of any number of Candida found in the urine. Theoretically, to differentiate an upper urinary tract candidiasis from a lower one, it would be necessary to catheterise the ureters and determine the presence of the fungi in the upper tracts. But from a practical standpoint, we do not feel this study is necessary, and we treat these patients with vesical washings. Only if this treatment fails to clear the mycosis is it justifiable to think about a possible renal candidiasis which should be treated with intravenous Amphotericin B (Harbach, 1970).

Bladder Washings.—All kinds of unsuccessful treatments have been used for monilial cystitis, but it was Goldman (1960) who first reported the use of Amphotericin B irrigations to treat this condition. Orally, Amphotericin may be partly absorbed by the bowel and when given intravenously may accompanied by a toxic reaction. According to Weinstein, only 2-5 per cent of the drug administered is eliminated in active form by the urine. For this reason the logical method of treating candidial cystitis is by vesical lavage. We have used a concentration of 20 mg. of Amphotericin B in 100 ml. of distilled water. Goldman reported good results employing 15 mg./100 ml. in one case, and 15 mg./400 ml. in another. Taking into account the fact that Candida is destroyed by concentrations of 0·03-1·00 mcg./ml., we have used a 200 times stronger solution than necessary. As solvent we have employed distilled water, but 5 per cent dextrose in water is also a good solvent. Saline should not be employed because it precipitates the Amphotericin. The solution should be protected from the light and kept in a refrigerator, because it is unstable at 37°C. The length of treatment should be 6-10 days.

SUMMARY

1. Candidiasis affecting the urinary bladder is relatively common.
2. Some of the reasons that favour the increasing incidence of this mycosis are:

(*a*) The indiscriminate use of broad-spectrum antibiotics.

(*b*) The presence of a larger number of patients with lowered biological resistance due to the disease itself or its treatment.

(*c*) Instrumental manipulation, favouring the contamination of vital organs.

3. Vesical candidiasis does not carry the dangers of renal localisation, but produces uncomfortable symptoms, resistant to usual antibiotic therapy and in some cases necessitating surgical intervention. Also spread by the ascending route may promote renal candidiasis.

4. Vesical lavage with Amphotericin B solution is easy to perform, highly effective and produces no toxicity.

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CHRONIC URINARY PSEUDOCYST

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AN encysted collection of urine is an uncommon occurrence which follows injury to a kidney or ureter resulting in extravasation of urine into the surrounding tissues. In the absence of drainage or infection, the urine mass may be enclosed by inflammation and organisation of the surrounding connective tissue. Such a mass usually presents clinically within days or weeks of the injury, but it may become chronic and present months or years later. In this paper we present 2 cases of chronic urinary pseudocyst, 1 of which presented 7 years after ureteral surgery. In our second case a ureteral obstruction was present and its relief permitted salvage of the involved kidney.

CASE REPORTS

Case 1.—A male, 36 years, was admitted to hospital for investigation of gross hæmaturia and urinary infection. Seven years before, in Holland, a left lower ureterolithotomy had been performed and the urologist reported that he had recovered uneventfully. On examination there was a well-healed scar in the left lower quandrant of the abdomen and deep to this a firm, non-tender mass was palpable. An intravenous pyelogram was not done because of sensitivity to the iodine dye. A cystoscopic examination was performed and the left side of the bladder was displaced medially, although the trigone was not distorted. A right retrograde pyelogram was normal. The left pyelo-ureterogram (Fig. 1, A) showed a hydronephrosis and hydro-ureter and the lower end of the ureter

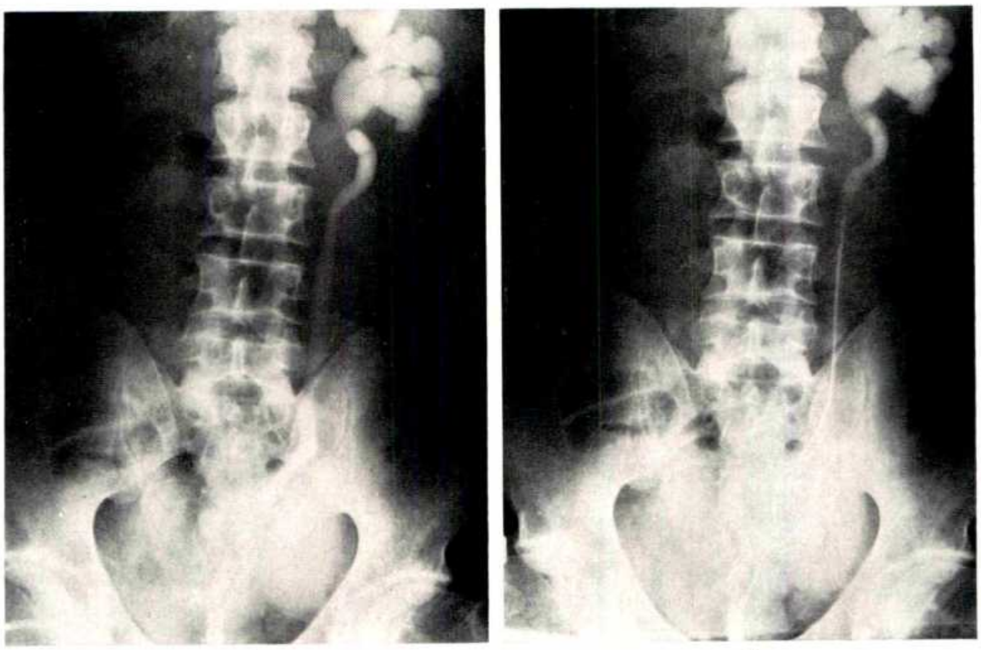

FIG. 1

A, A retrograde pyelogram shows an obstructed left kidney and ureter with medial displacement of the lower end of the ureter. B, A later film of the pyelogram shows dye in the cystic mass in the left pelvis.

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was displaced medially. The last film of the retrograde (Fig. 1, B) showed dye in a cystic space to the left of the bladder. This dye could only have come from that injected into the ureter, indicating an opening between the ureter and the cyst. A cystogram was done immediately, (Fig. 2, A and B) and the cyst could be seen to displace and distort the bladder by pushing in its left side. No further dye entered the cystic space during the cystogram. Radioactive isotope studies indicated very little function of the left kidney and this with the retrograde pyelogram indicated a badly damaged left kidney.

At operation the mass was exposed through an incision extending from the left flank to the suprapubic area. It filled the left side of the pelvis and was densely adherent to the peritoneum, external iliac vein, pelvic wall and bladder. The mass was incised and its cystic structure confirmed. Its wall was several millimetres thick and it contained clear yellowish fluid. A culture of this fluid showed no bacterial growth. Several strands of tissue ran across the cavity like struts and the thickest of these was the lower portion of the ureter. It was thickened and indurated in its intracystic course. The upper portion of the ureter was dilated and its wall was thick and rigid, while the kidney was scarred and contracted. A nephro-ureterectomy was done. A portion of the cyst wall was resected, but that part adherent to surrounding structures was not disturbed. A soft rubber drain was left in place for 10 days, but there was little drainage. The wound healed well and his recovery was uneventful.

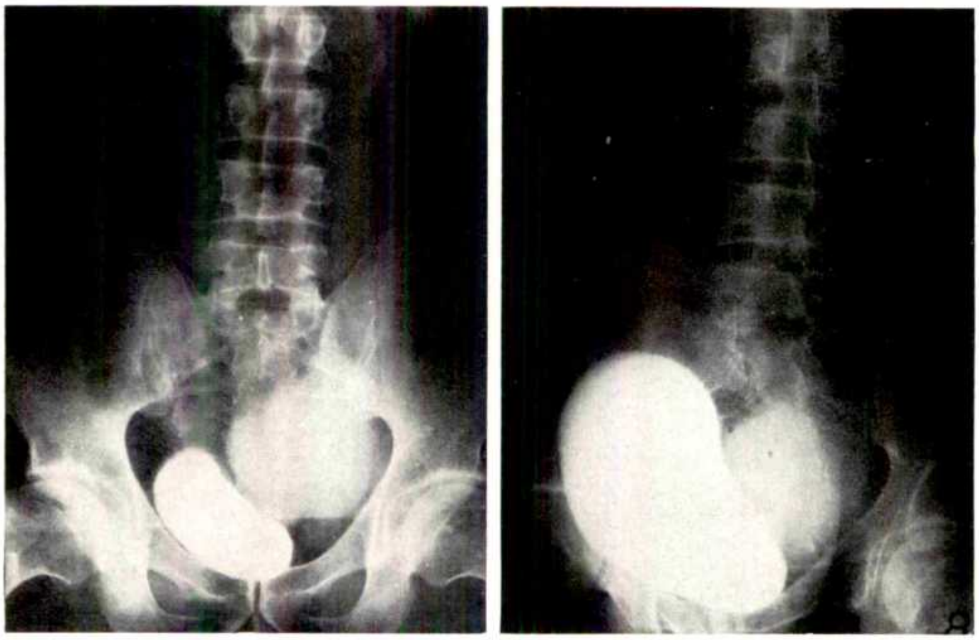
A B

FIG. 2

A and B, A cystogram after the retrograde demonstrates the relation of the bladder to the cystic mass.

Comment.—In our opinion this pelvic cyst was a chronic urinary pseudocyst of 7 years' duration, since the only "injury" to the urinary tract was the ureterotomy 7 years previously. Although the wound was drained for several days, a pocket of urine must have collected around the ureter and developed into a pseudocyst. The ureter ran across the middle of the cavity for a distance of 2·5 inches. Our pyelogram indicated a communication between the ureter and the pseudocyst. The ureter was obstructed and a hydronephrosis and severe renal damage resulted.

Case 2.—A female, aged 60, was admitted to the hospital with right abdominal discomfort. She dated this symptom to a minor car accident 4 months previously. The pain had developed slowly but was not disabling. She also complained of postcoital vaginal bleeding. Physical examination showed a mass occupying the right side of her abdomen, extending from the costal margin into the right iliac fossa. It was smooth, dull to percussion and non-tender. Vaginal examination revealed a hard, irregular cervix with induration extending into the base of the right broad ligament.

An intravenous pyelogram did not show any kidney function on the right side, although the left was normal. The mass displaced the ascending colon to the left. It was not calcified. Retrograde pyelography (Fig. 3) revealed a hydronephrotic right kidney, which was displaced superiorly and medially. The ureter was moderately dilated down to the paravesical area, where a narrow segment indicated a stricture. A renal angiogram (Fig. 4) demonstrated a normal left kidney and upwards displacement of the right kidney by the mass. The smaller renal arteries were decreased in number but there were no tumour vessels.

A biopsy of the cervical lesion was performed and a squamous cell carcinoma diagnosed. Its spread into the right parametrium made it a stage III. During the subsequent operation the pelvic organs were examined and the tumour was found to involve the base of the right broad ligament. This tumour was obstructing the lower end of the right ureter. The carcinoma of the cervix was treated by external Cobalt irradiation, since a stenotic cervix prevented endocervical radium therapy.

The abdominal mass was explored through a right eleventh-rib incision. A large cystic structure was found in the retroperitoneum. It extended from the diaphragm to the pelvis and contained 6,000 cc. of clear amber fluid. The kidney was displaced upwards and medially and surrounded by scar tissue, which made up a portion of the wall of the pseudocyst. The ureter was pushed medially and, along with the inferior vena cava, was bound down and fixed by the fibrous wall of the pseudocyst. The kidney and ureter were left in place and about one-quarter of the wall of the pseudocyst was removed. Drains were placed in the cavity. The pseudocyst wall was composed of dense, fibrous tissue with no epithelial or endothelial lining.

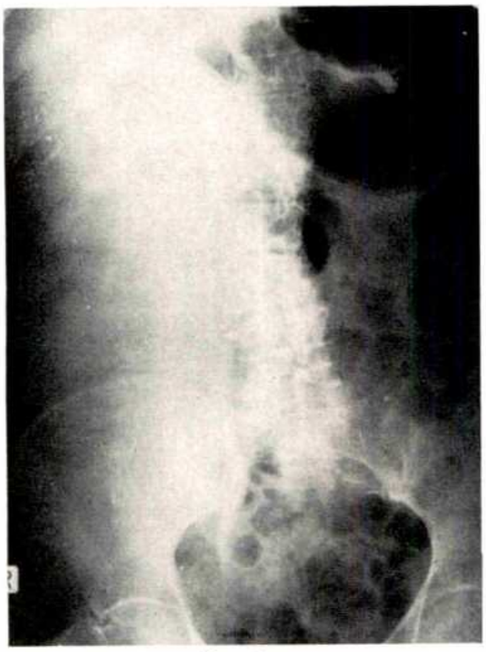

FIG. 3

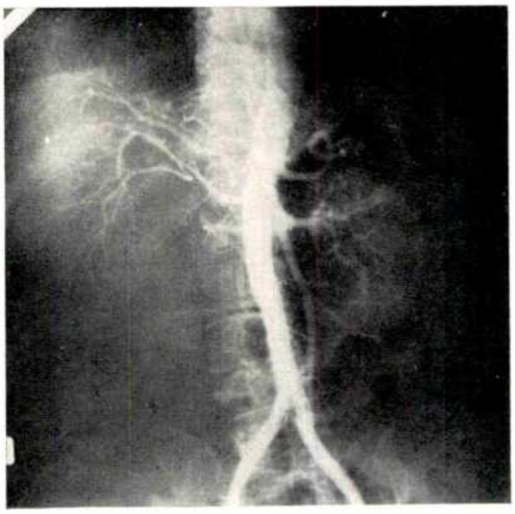

FIG. 4

Fig. 3.—A retrograde pyelogram shows the mass in the right abdomen displacing the obstructed right kidney. The right ureter is stenosed at its lower end.

Fig. 4.—A renal angiogram shows the vasculature of the displaced right kidney. The large mass is avascular.

There was copious drainage of clear, yellowish fluid from the cavity for a week, but it gradually decreased and stopped by the seventeenth day. The fluid contained creatinine 15 mg. per cent, sodium 57 m.Eq./l., potassium 13 m.Eq./l., chloride 49 m.Eq./l., and protein 700 mg./24 hours. We judged that it was urine.

The patient recovered and is well to date. The cervical and parametrial mass disappeared after the radiation therapy. Six months post-operatively an intravenous pyelogram showed a slight but definite secretion of dye by the right kidney. There was no evidence of hydronephrosis.

Comment.—This patient's right kidney was undoubtedly lacerated in the automobile accident 4 months before diagnosis, when she struck her abdomen against the car's dashboard. Coincidentally, her right ureter was obstructed by the cervical cancer, and this combination of events resulted in a continued leak of urine from the kidney, with formation of the urinary pseudocyst. After drainage of the pseudocyst, urinary drainage from the kidney persisted for 2 weeks. The cervical carcinoma was radiated during this period of time, with relief of the ureteral obstruction and cessation of the urinary leakage. The kidney, which appeared to be non-functioning by pyelography and radioactive isotope studies, recovered its function (intravenous pyelogram) several months later.

DISCUSSION

The first such case reported was described as a pararenal pseudohydronephrosis by Hawkins in 1834. The patient was a boy who suffered a lacerated renal pelvis when run over by a horse and cart. Crabtree, in 1935, collected 20 cases of pararenal pseudocyst from the literature of the previous century and added 3 cases of his own. Bartley *et al.* (1966) reported a case of para-ureteral pseudocyst associated with a lacerated ureter sustained in a motor vehicle accident. His review of such cases presented in the literature suggested that para-ureteral pseudocysts are much less common than the pararenal type.

These cystic structures develop following a laceration of the urinary collecting system with extravasation of urine into the surrounding connective tissue spaces. Usually, such urinary extravasation manifests itself promptly by the resulting inflammatory reaction. Surgical drainage and repair of the damaged ureter or kidney usually follows. In pseudocysts the mass of urine is not drained but is contained by the surrounding organising inflammatory tissue and the cystic mass results. If the kidney is lacerated the intact perinephric fascia may contain the leaking urine. Razzaboni (1922) produced pseudocysts in rabbits and dogs by sectioning the ureter and closing the surrounding fascia around the ureter. An ill-defined fibrous sac formed around the extravasated urine in 12 days, but the pseudocyst wall and mass were not well-defined until 3 to 6 weeks had passed. Crabtree suggested that an obstruction of the affected ureter was necessary for a pseudocyst to form and this was so in one of our cases.

The pseudocysts may appear in a matter of weeks, but can manifest themselves years later. Our first case was diagnosed 7 years following ureteral trauma. Johnson and Smith (1941) reported a case of 37 years' duration. In Crabtree's series the majority of cases presented in 1 to 5 weeks. Pseudocysts which follow renal reconstructive surgery or severe renal trauma usually appear and are diagnosed within a matter of days or weeks. Khonsari *et al.* (1971) reported such cases following a case of pyeloplasty and another of renal trauma. But in mild cases of renal trauma treated conservatively or not at all, such an abdominal mass may develop slowly and the diagnosis will not be readily apparent.

The chronic urinary pseudocyst is treated surgically. Drainage of the cyst and excision of that part of its wall which can be easily mobilised is not difficult. But most of the pseudocyst wall is densely adherent to the surrounding tissues and organs, and resection of the wall with possible damage to such structures is unnecessary. The affected kidney and ureter may be obstructed and badly damaged if the pseudocyst is long-standing, and nephrectomy or nephro-ureterectomy is indicated in such instances. In earlier cases Khonsari advocates repair of the affected kidney or ureter with nephrostomy drainage. Certainly, if the primary or secondary ureteral obstruction can be removed and if the kidney is not severely damaged, salvage of the renal unit should be attempted.

Such terms as pseudohydronephrosis, hydrocele renalis and perirenal or perinephric cyst have been used to describe this entity in the past. Chronic urinary pseudocyst is the most accurate pathologic and descriptive term. Its anatomic site can be denoted by the terms, pararenal, para-ureteric or paravesical.

SUMMARY

Two cases of chronic urinary pseudocyst are reported; one 4 months and the other 7 years in duration. Renal damage was severe in both cases, but relief of ureteral obstruction in one case resulted in salvage of the affected kidney.

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POSTERIOR URETHRAL VALVE

Problems in management of the Upper Urinary Tract

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INCREASING awareness of posterior urethral valves in the ætiology of bladder outlet obstruction and wider use of voiding cysto-urethrograms have resulted in more frequent diagnosis of this condition. It is now generally agreed that urethral valve is the most common cause of lower urinary tract obstruction in infants and children. In an infant presenting with symptoms soon after birth, the obstruction is generally more severe and the damage to the upper urinary tract is already extensive. A child with a lesser degree of obstruction and a more gradual back pressure effect on the kidneys is usually older before any symptoms become apparent.

Tolmatschew, in 1870, was the first to define and discuss urethral valves. Young, in 1919, made the first clinical diagnosis and later described three types of valves. Williams and Eckstein (1965) presented their extensive experience, but dealt meagrely with the management of upper urinary tract pathology, which constitutes a major problem in these unfortunate children.

Our experiences in the diagnosis and management of 32 cases of posterior urethral valve is presented. We have included in the present study only patients with proved obstructive valves except in one, a new-born, who had associated umbilical fistula. The problems encountered in management of the upper urinary tract, in relation to vesico-ureteral reflux, grossly dilated ureters and secondary uretero-pelvic obstruction, are discussed.

Incidence.—The increasing frequency with which urethral valves have been recognised is revealed in Figure 1. Out of 32 cases, 25 (78·1 per cent) have been diagnosed during the last five years.

Pathology.—All the valves in the present series correspond to Young's type I, except in 3 patients who had type III valve. Two of these were diagnosed at autopsy. Hydronephrosis and dilatation of the ureters were noted in 25 cases. In 14 of them the ureters were grossly dilated and tortuous (Fig. 2).

Presentation.—Approximately half of the cases presented in the first 2 years of life. All the 7 fatal cases fall into this age group (Fig. 3). The oldest case was 13 years of age.

Table I shows the various modes of presentation, the most common presenting feature being urinary tract infection and dribbling or incontinence.

Poor stream of urine and palpable bladder have been noted in the majority of our patients and the kidney was palpable in 14 cases (43·7 per cent). It was interesting to note visible peristalsis of grossly dilated and tortuous ureters in 3 patients (Table II). Well developed renal rickets has been noted in 3 cases.

Blood urea level at the time of presentation is shown in Figure 4. It was raised above 100 mg. in 6 patients. Urine culture was positive with significant colony count in 17 patients, coliforms and proteus being the most common bacteria. In 5 patients, more than one organism was grown in culture (Fig. 5).

Diagnosis.—In 27 patients the diagnosis of posterior urethral valve was made by voiding cysto-urethrogram. In 1 patient it was based entirely on endoscopy. In the remaining 4 cases autopsy confirmed the diagnosis.

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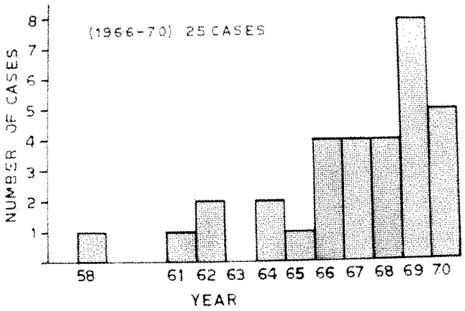


FIG. 1

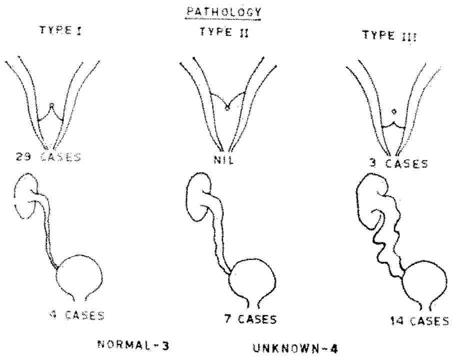


FIG. 2

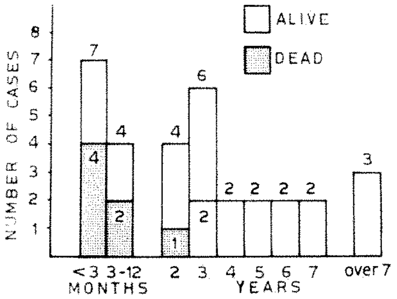


FIG. 3

Fig. 1.—Urethral valve —showing rise in incidence.

Fig. 2.—Pathology.

Fig. 3.—Age incidence and mortality.

TABLE I

Mode of Presentation

	No. of cases
Recurrent urinary infection	8
Dribbling or incontinence	7
Dysuria and frequency	3
Vomiting	3
Failure to thrive	3
Hæmaturia	2
Others	6

TABLE II

Physical Findings

	No. of cases
Poor stream of urine	25
Palpable bladder	23
Palpable kidney	14
Abdominal distension	7
Visible ureters	3

Intravenous urography was performed in 21 patients (Table III). In 14, bilateral hydronephrosis and dilatation of the ureters were noted, but in the majority the dilatation was more advanced on one side.

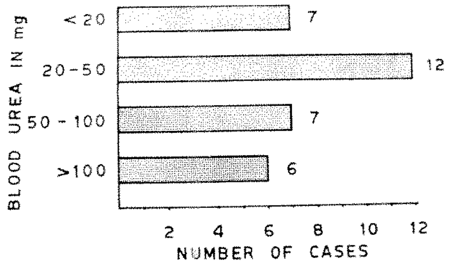


FIG. 4
Blood urea level.

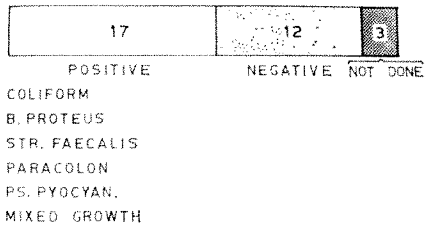


FIG. 5
Urine culture results.

TABLE III

Excretory Urogram—Total 21 Cases

	No. of cases
Bilateral hydronephrosis and hydro-ureters	14
Unilateral hydronephrosis and hydro-ureter	1
Normal kidneys and ureters both sides	2
Non-visualisation—both sides	1
Hydronephrosis and hydro-ureter on one side and non-visualisation on other side	3

TABLE IV

Voiding Cysto-urethrogram—27 Cases

Findings	No. of cases
Bilateral vesico-ureteral reflux	7
Unilateral vesico-ureteral reflux	6
Dilatation of posterior urethra	26
Bladder neck-filling defect	15

TABLE V

Preliminary Urinary Drainage Procedure

Drainage operation	No. of cases
Nephrostomy	2
Ureterostomy	3
Suprapubic cystostomy	7
Urethral catheter	3

Voiding cysto-urethrograms were performed in 27 patients. Reflux was demonstrated in 13, and in 7 it was bilateral (Table IV). The refluxing ureters showed gross dilatation and tortuosity. All three nephrectomies were done on the side showing grade IV reflux.

Pre-operative Treatment.—Correction of biochemical disturbances and adequate pre-operative drainage gains priority over the actual extirpation of the valves. Preliminary drainage procedure was undertaken in 14 patients (Table V). Nephrostomy was done in 2 patients and bilateral loop ureterostomy in 3, and all these patients improved remarkably. Suprapubic cystostomy was done in 7 cases, but improvement in general was not consistent.

Surgical Treatment.—The various approaches used for extirpation of valves are shown in Table VI. We believe that transurethral resection fulguration of the valves is the easiest and most efficient. Perineal excision of the valves has been a good alternative. The retropubic approach appears to be technically extensive.

TABLE VI

Operation for Valves in 20 Cases

Operation	No. of cases
Transurethral resection	7
Perineal excision	7
Retropubic approach	2
Rupture of valve-bouginage	4

Bladder neck resection, transurethral or transvesical and bladder neck Y-V plasty was done in 12 of the earlier cases with the belief that the prominent posterior lip seen on cysto-urethrograms is also obstructive. Resection of the dome of the bladder was done in 1 patient only, where after successful excision of the valve, the bladder remained atonic with a large residue (Table VII).

TABLE VII

Other Operative Procedures

	No. of cases
Anti-reflux procedures	7
Reconstruction of ureter	3
Bladder neck Y-V plasty	3
Bladder neck resection: Transurethral . . .	3
Transvesical . . .	6
" Domectomy "	1
Nephro-ureterectomy	3

Management of Upper Urinary Tract.—Three patients had a nephro-ureterectomy for pyonephrosis of the non-functioning kidneys. Anti-reflux operations, using the Leadbetter-Politano technique, were performed in 7 patients (13 ureters). In 3 patients (5 ureters), this procedure was combined with operation to straighten the tortuous ureters and sleeve resection.

RESULT OF SURGICAL TREATMENT AND FOLLOW-UP

Twenty patients have undergone surgery for valves. One patient with a type III valve, where the pathology seemed more like a stricture, was treated with periodic urethral dilatation. In 2 patients the parents refused surgery and 2 other patients are awaiting surgical treatment.

Of the 20 patients operated upon for valves, 4 have been lost to follow-up. The remaining 16 have been followed up for periods varying from 2 months to 8 years (Fig. 6). Fifteen of them have good urinary control. Only 1 patient has nocturnal bed-wetting. Six patients have maintained sterile urine. The other 10 have positive urine cultures responding to antibiotic therapy, but show no clinical evidence of infection.

Study of pre-operative and post-operative serum creatinine and electrolyte estimation in 12 patients revealed that renal function has improved or been maintained in all these patients (Table VIII).

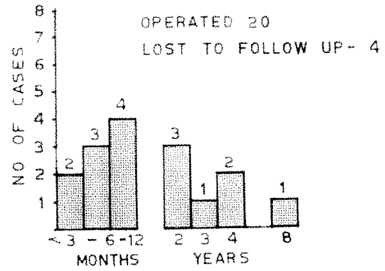


FIG. 6
Period of follow up.

TABLE VIII

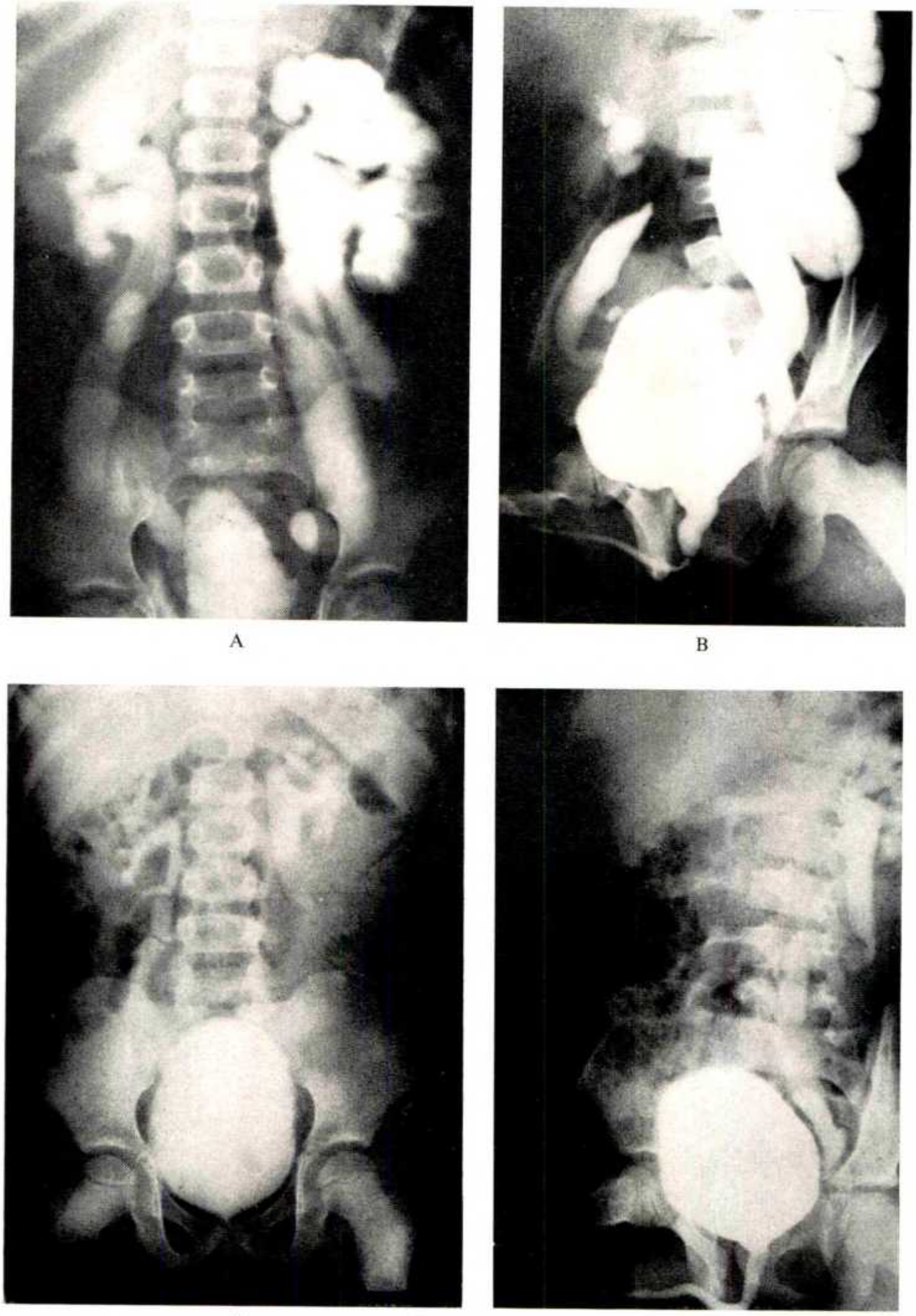
Pre-operative and Post-operative—in 12 Cases

		Pre-op.	Post-op.
Serum Creatinine in mg.			
	Below 1	3	5
	1-2	8	7
	Over 2	1	0
Electrolyte in mEq.			
Potassium	below 5	7	10
	5 and above	5	2
Bicarbonates	20 and above	8	10
	Below 20	4	2

Excretory urograms have been carried out during the follow-up period in 14 patients. Six patients have shown remarkable regression in dilatation of the upper urinary tract, but in 4 of these vesico-ureteral reflux persists (Fig. 7). The remaining 8 patients showed no appreciable radiological improvement. Seven of these patients had anti-reflux procedures including three who had sleeve resection of the ureters (Fig. 8). The follow-up in the latter group is short and will form part of another paper on " Problems of large ureters in children ". Only 1 patient has shown evidence of secondary pelvi-ureteral obstruction after reconstruction of the ureter and is awaiting surgery (Fig. 9). Marked dilatation of the posterior urethra seen on voiding cysto-urethrogram regressed completely after adequate resection of the valves (Fig. 10).

DISCUSSION

In male infants and children presenting with poor stream of urine, incontinence, recurrent urinary infection or a palpable bladder, the possibility of urethral valves should always be kept in mind. The diagnosis can be easily confirmed by micturating cysto-urethrograms. The damage to the upper urinary tract is more severe when the patient presents in infancy and early childhood. The mortality in this group still remains formidable. The grossly dilated and tortuous ureters are often the seat of secondary obstruction and form an important pathological entity in cases of urethral valves. When such cases have renal insufficiency, or are associated with acute urinary tract infection, it is mandatory that the upper urinary tract is drained adequately. The best preliminary drainage procedure is loop ureterostomy, which helps in the improvement of renal function as well as in regression of hydro-ureteronephrosis. Destruction of the urethral valve is accomplished by transurethral fulguration or by the open perineal approach. Although the posterior lip of the bladder neck appears prominent, suggesting secondary bladder neck obstruction, this appearance in the cysto-urethrogram is due to dilatation of the posterior urethra and

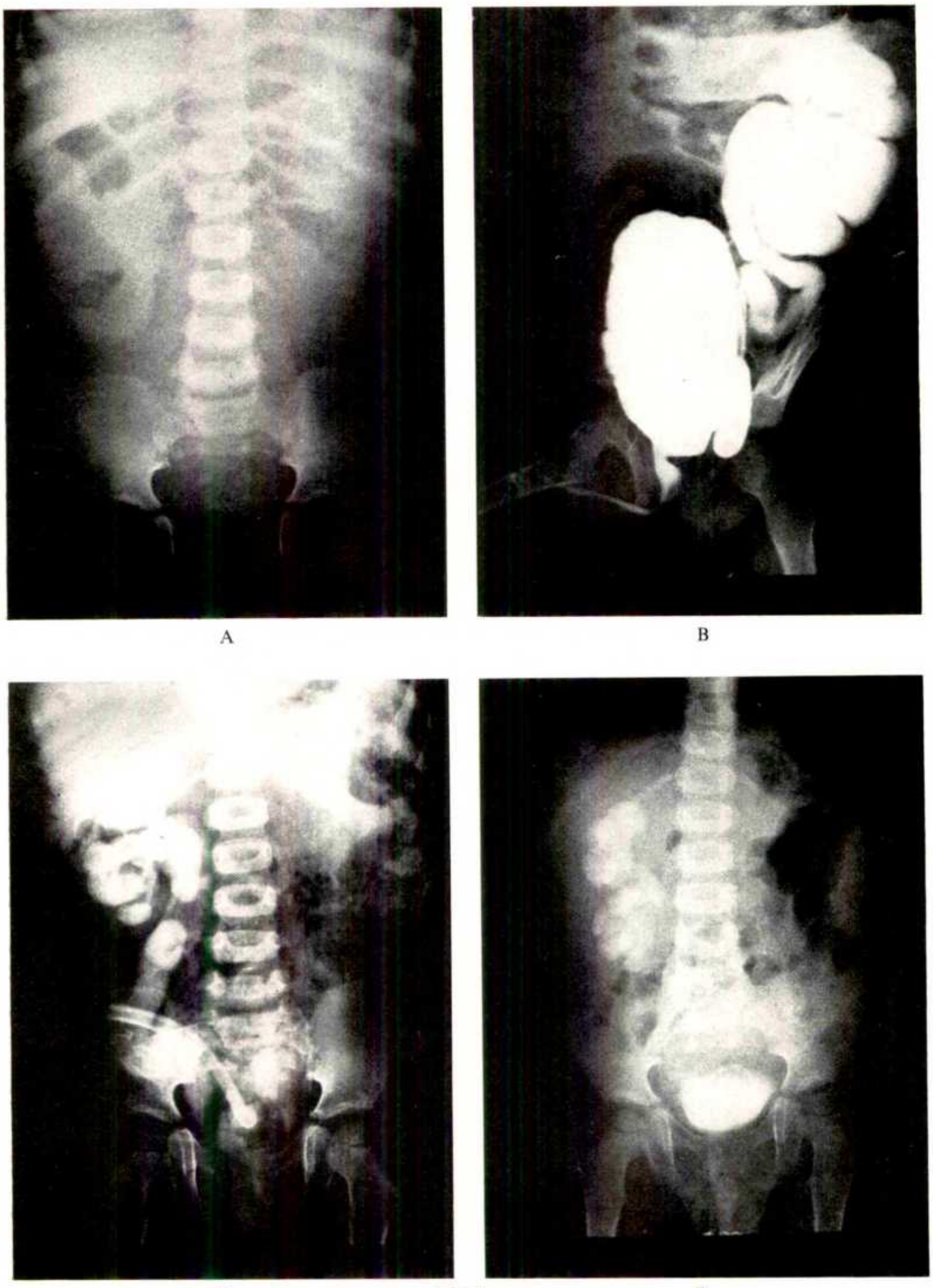


A B

C D

FIG. 7

A, Infusion pyelogram in a boy aged 6 years shows bilateral hydronephrosis, gross dilatation and tortuosity of ureters. B, Voiding cysto-urethrogram shows evidence of urethral valve with dilatation of posterior urethra. Grade IV vesico-ureteral reflux is seen on both sides. C, Post-operative excretory urogram following perineal excision of valve showing remarkable regression of upper urinary tract dilatation. D, Post-operative voiding cysto-urethrogram showing normal urethral calibre but persistence of reflux.



A B

C D

FIG. 8

A, Excretory urogram in a 4-year-old boy with palpable kidneys, ureters and bladder showing only nephrographic effect on right side. B, Voiding cysto-urethrogram in the same patient. C, I.V.P. following excision of valve and bladder neck resection shows persistence of upper urinary tract dilatation on the right side. Left nephrostomy followed by nephro-ureterectomy was done for pyonephrosis in non-functioning kidney. D, I.V.P. after sleeve resection and tunnel re-implantation of right ureter shows appreciable regression in hydro-ureteronephrosis.

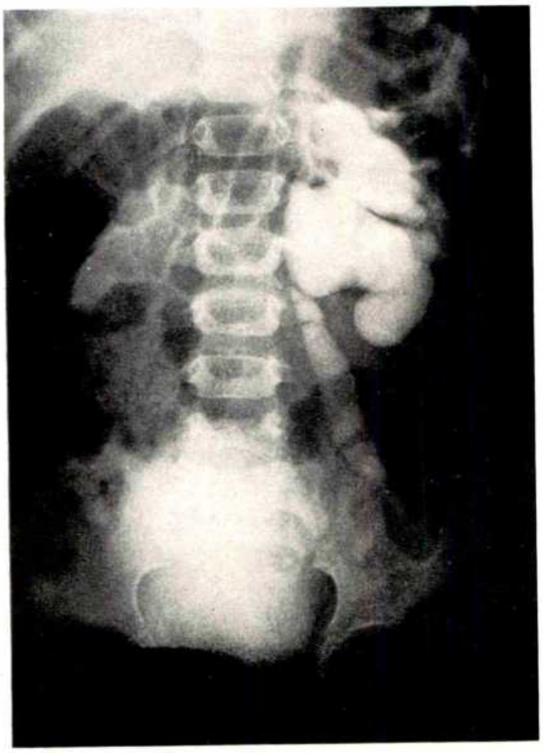
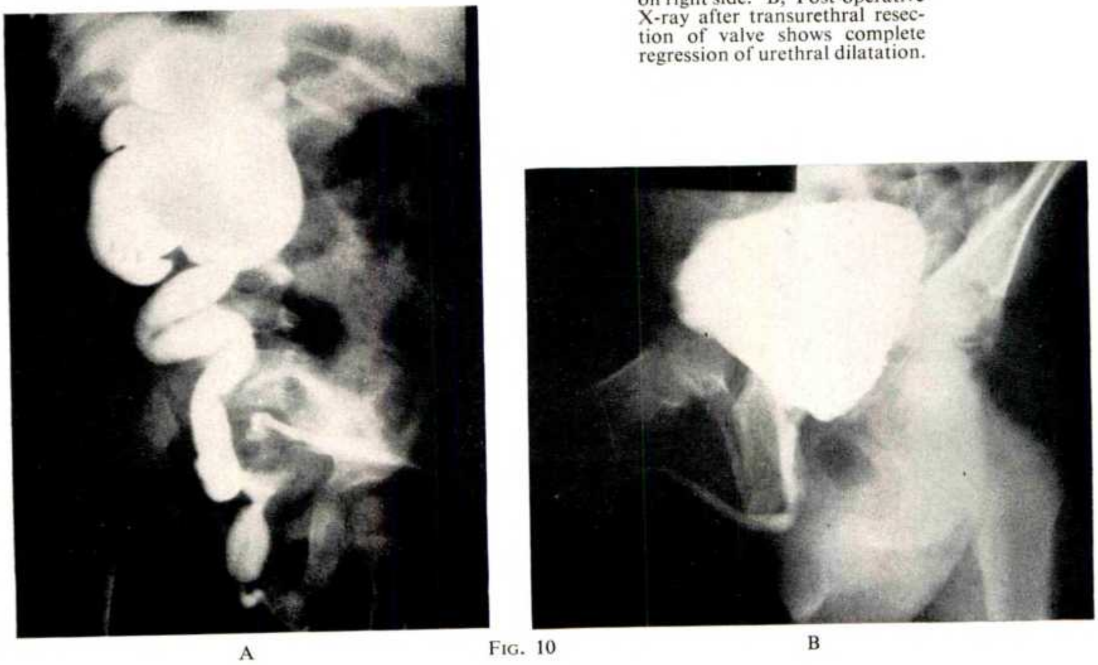


FIG. 9

Fig. 9.—Excretory urogram after shortening and sleeve resection of grossly dilated and tortuous left ureter shows persistence of hydronephrosis due to secondary uretero-pelvic obstruction.

Fig. 10.—A, Pre-operative micturating cysto-urethrogram showing prominent urethral valve and gross dilatation of posterior urethra. Reflux is seen on right side. B, Post-operative X-ray after transurethral resection of valve shows complete regression of urethral dilatation.



A FIG. 10 B

this feature disappears after surgery on the valves. Thus, we believe that bladder neck resection in these cases is not necessary. In a significant number of cases destruction of the valve alone is adequate and dilatation of the upper urinary tract regresses. In others, where hydronephrosis and dilatation of the ureters persist, with or without vesico-ureteral reflux, re-implantation of the lower end of the ureters with anti-reflux procedure has to be considered. A few cases, where the grossly dilated and tortuous ureters do not drain well, may require straightening and sleeve resection of the ureters. Rarely, hydronephrosis due to co-existing uretero-pelvic obstruction may persist after the above surgical corrections and may require pyeloplastic procedure. We have, as yet, no final answer for these unfortunate children born with posterior urethral valve with gross dilatation of ureters. We have recently heard of total correction of such a grossly anomalous urinary tract. Our experience with such formidable operative procedure is limited to 3 cases. The immediate results have been encouraging. Preliminary drainage of obstructed kidneys, destruction of the urethral valve, anti-reflux procedure with or without sleeve resection of the ureter and, rarely, correction of secondary uretero-pelvic obstruction form a continuum in the management of many of these cases.

SUMMARY

Our experience with posterior urethral valve in 32 cases, with emphasis on problems in the management of the upper urinary tract is reported.

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INCOMPLETE DUPLICATION OF THE MALE URETHRA

Report of an Unusual Case

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DUPLICATION of the male urethra without associated malformations is rare. It is usually part of a more complex anomaly, a double bladder and/or double phallus, and has been seen with duplication of the colon. When it occurs within a single penile shaft it can be *complete*, with both urethræ originating independently from one bladder, having two different courses in the penis and two meatuses, or incomplete, in which one or more short accessory channels develop from the normal urethra.

Since the first observation by Aristotle of a man with two urinary streams, many cases of complete duplication have been reported. An excellent review of the literature was done by Gross and Moore in 1950. Later Casselman and Williams described 4 cases of complete duplication in the male (1966). Since then Olsen (1966), Tripathi and Dick (1969) and Karanjavala (1970) have each reported a single case, bringing the total to 41 published, while a few hundred patients with incomplete urethra have been described. In this article an unusual case of incomplete duplication is presented.

Case Report.—In 1970 a 17-year-old Caucasian boy was referred to the University of California, Los Angeles, because of recurrent episodes of cystitis and bilateral epididymo-orchitis for the last 2 years. He had urinated since birth from an opening on his perineum with only a few drops coming from a normally located urethral meatus. There was no urinary incontinence and when ejaculation occurred most of the semen came out through

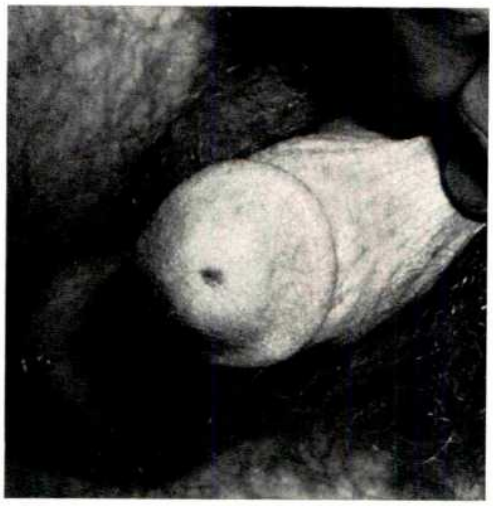

FIG. 1

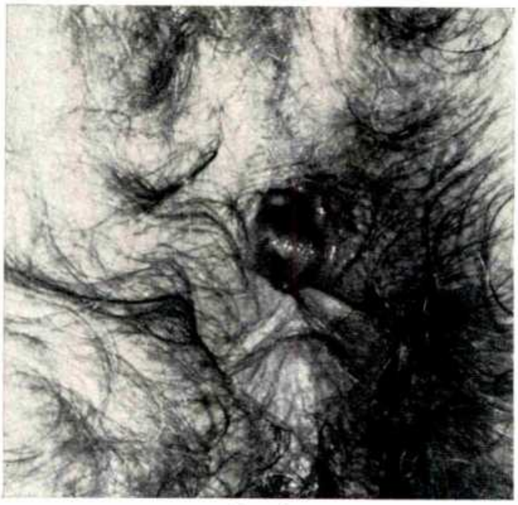

FIG. 2

Fig. 1.—Penile urethral meatus.

Fig. 2.—Opening of the accessory urethra on to the perineum, just anterior to the anus.

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the perineal opening with only a small amount through the normally located urethral meatus. There was no deviation or angulation of the penis during erection.

The past history was non-contributory and physical examination was normal except for the genitalia and perineum. The anatomically placed urethral meatus was very small, but appeared otherwise normal (Fig. 1). Both testicles were in the scrotum. The left was normal with only a slightly indurated and tender epididymis. The right was small and soft with an indurated but not tender epididymis.

In the perineal area, just anterior to the anus, there was an opening about 1 cm. in diameter, lined by normal urethral mucosa without any signs of inflammation (Fig. 2). Rectal examination showed good sphincter tone with no masses, tenderness or bleeding present. The prostate, which was firmer than normal, felt like 2 bands going upward, almost like 2 separate prostates.

The urinalysis showed 3-4 WBC, no RBC and no visible bacteria. The urine culture revealed, however, E. coli greater than 100,000/ml., sensitive to Ampicillin.

A voiding cysto-urethrogram showed a large, slightly pear-shaped bladder, with no definite intrinsic abnormality; during voiding most of the radiopaque fluid passed through the perineal urethra which had the appearance of a female type of urethra. At a later stage of voiding a second urethra with a fine lumen coming from the region of the prostatic urethra, and extending into the penile urethra along its full length, was seen.

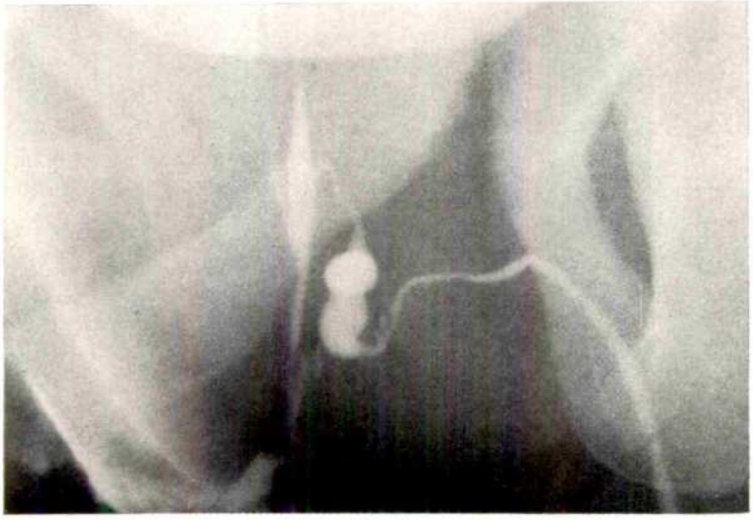

FIG. 3

Retrograde penile urethrogram. For explanation see text.

A retrograde penile urethrogram was done to demonstrate the second urethra more adequately. The penile urethra was small and thin but patent (Fig. 3). At the level of the bulbous and prostatic urethra it became wider and more normal in appearance and the indentation of the sphincter could be seen. At that point the channel extended into the perineal (prostatic) urethra by a very fine duct which looked almost as though it were one of the ejaculatory ducts. Cysto-urethroscopy was performed through the perineal opening; it was not possible to pass any cystoscope into the penile urethra. The perineal urethra appeared feminine in contour, but was longer and of larger diameter than the average adult female urethra. There was no visible verumontanum, but a midway sphincter was present. On the lateral wall, distal to this sphincter, there was also a hyperæmic area that appeared like the possible opening of the penile urethra. The bladder mucosa showed chronic inflammatory changes with normal ureteral orifices and bladder neck.

The patient was treated with antibiotics and no attempt was made at this time to correct this anomaly.

DISCUSSION

This case is classified as an *incomplete duplication*, because the two urethra do not have a common exit from the bladder. The unusual features of the case, however, are that the perineal urethra, which appears to be the accessory one: (1) communicates directly with the bladder, while the penile urethra does not, (2) is more functional than the normal or penile urethra, (3) communicates with both the bladder and the normal urethra, and (4) opens into the perineum in a manner similar to that we have observed in patients with congenital agenesis of the penis.

When Gross and Moore reviewed the literature in 1950 they reported only a few cases in which the accessory channel opened on the ventral surface of the penis or into the perineum. None showed a communication with the bladder, regardless of the length of the tract. Rinker in 1943 reported a case in which there was a very long, ventral accessory urethra which " ran upward between the bladder and the rectum, terminating blindly just below the right iliac vessels ", and which did not have any communication with the bladder or the normal urethra. In our case not only was there a communication with the bladder, but also with the normally appearing urethra.

Boissonat in 1961 reported the first case of an accessory urethra in a hypospadic position which was more functional than the normal. The dorsal urethra, however, opened into the bladder, so that there was a complete duplication with no communication between the 2 channels. The findings on rectal examination were very interesting. The author says, " the prostate was found to be normal and small, a little more depressed than usual on its middle, perhaps from lack of prostatic tissue behind the postero-inferior urethra ". In our case we had the impression that the prostate was made up of 2 bands extending upward almost like 2 separate prostates. Karanjavala in 1970 described a similar case of an accessory channel, more functional than the normal, which originated from the bladder neck and terminated at the anterior anal margin. In this case, also, there was a complete duplication and the 2 channels did not communicate except at the bladder neck. Williams (1968) also described 3 similar cases.

There are 2 unanswered questions regarding our case: (1) Which is the normal urethra, and where is the communication between the 2 channels? How can we explain this particular case in view of the present theories regarding the embryological error that leads to a duplication of the urethra?

We did not instrument the penile channel, but radiologically it appears to be a normal but smaller and thinner urethra with an indentation of the external sphincter. Proximal to this point there is only a fine duct, similar in appearance to an ejaculatory duct, which connects the penile to the perineal urethra. On the other hand, the perineal channel appears like a feminine urethra; it does not have a visible verumontanum and has a sphincter in its mid-portion. It is unusually larger and appears to be the accessory urethra more than the normal urethra. It does, however, carry semen during ejaculation. This suggests that the 2 channels join in the prostatic urethra, probably through an ejaculatory duct, so the semen can go through the normal and also through the less resistant route, the perineal channel. This can also explain the history of the patient, who sought medical attention only because of repeated episodes of epididymitis. The poorly functioning penile urethra is a reservoir of bacteria that are only partially washed out during urination and are thus the source of epididymal infection. In fact, when the patient came to our observation he did not complain of any lower urinary tract symptoms, but a voided urine specimen showed the presence of E. coli more than 100,000/ml., probably due to contamination of the specimen by the urine passed through the penile channel.

Many embryological explanations for duplication of the urethra in a single penile shaft have been discussed in the literature:

1. Bifurcation of the urethral anlage because of an abnormal continuation of the splitting process of the urorectal septum.
2. Bifurcation of the urethral gutter.
3. Fusion of the paired buds of the genital tubercle too late in time and too far posteriorly.
4. A non-regressing cloacal membrane which prevents the mesoderm to reinforce the central portion of the abdominal wall below the umbilicus. This can result in exstrophy of the bladder, but may also explain a duplication of the urethra with dorsal chordee.

Casselman and Williams (1966) advanced these theories, but concluded that the anatomy of the malformation varies so widely from case to case that it is unlikely that the same embryological explanation can satisfactorily explain all cases.

Another theory is an inflammatory process which sealed the normal urethra distally and then caused a fistula or a canalised diverticulum. This can only in part explain our case. In fact, it does not explain how the accessory urethra or the fistula has a connection with the bladder, too.

One other interesting question is the treatment of this unusual case. Even if conservative management (antibiotic treatment) keeps the patient clinically uninfected, there may still be a necessity to do a reconstructive procedure for cosmetic reasons and in view of the reproductive possibility. In fact, if the patient has no surgical treatment he should probably inseminate his wife artificially.

In the literature the usual treatment in cases of duplication which required surgery has been the excision of the accessory urethra. Fulguration and/or injection of sodium morrhuate into the accessory channel has also been reported. This may be contra-indicated because it could cause or aggravate already existing chordee. In our case such procedures would not be desirable. It could be possible, however, to lay open the penile urethra, as in a first-stage Johanson Urethroplasty. The calibre of this channel is, in fact, too narrow to allow free urine flow. The dissection would have to be done all the way back to the perineum. We think that the sphincter that controls the boy's urination is very close to the bladder neck and it would be possible to dissect back to the dilated area of the penile urethra, suture the perineal urethra to this and make one single perineal opening, which would be further out into the perineum, more at the base of the penis, instead of just in front of the anus. A second stage could then establish a normal urethra anatomically with adequate calibre.

To date we have not urged reconstruction because of fear of possible incontinence or interference with the sexual activity of the patient.

SUMMARY

The authors report a case of unusual incomplete duplication of the urethra in a 17-year-old boy. Characteristic features are: (1) the accessory channel is more functional than the normal, (2) it opens into the perineum, and (3) it communicates with both the bladder and the penile urethra. No surgery was performed, but a suggestion of a possible reconstructive procedure is discussed.

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A RARE CONGENITAL MALFORMATION: NON-UNION OF THE TESTICLE WITH THE EPIDIDYMIS AND THE SPERMATIC DUCT

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FOLLIN in 1851 first described this congenital malformation and pointed out that it occurs in cases of clinical ectopic testis. Later, Badenoch (1946), Lazarus and Marks (1947) and Volozhin (1969) reported on similar cases.

As known, the embryological development of the genital organs is closely connected with the development of the urinary system. At the beginning the mesonephros serves as the main secretory organ; shortly afterwards, the gonadal folds appear as a thickening on the ventral aspect. Some of the mesonephric canaliculæ connect with the developing gonad so that the mesonephric duct also serves as a conduit for the genital cells. Later on, from the same canaliculæ, the epididymis develops and, after enveloping itself in a layer of smooth muscles, the spermatic duct also (Fig. 1). Malformations may occur as the result of arrest or changes in development, and Windholz (1923) classified these in 4 categories:

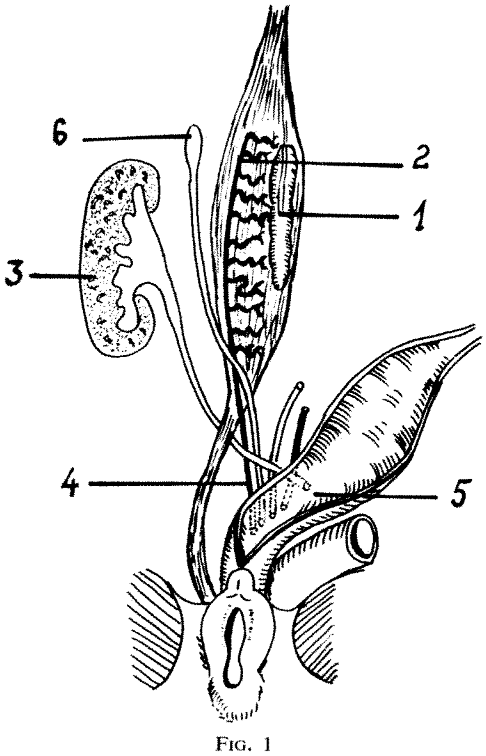

FIG. 1
Embryological development of the genito-urinary tract:
1. Primitive testis. 2. and 4. Mesonephric duct.
3. Kidney. 5. Urinary bladder. 6. Mullerian duct.

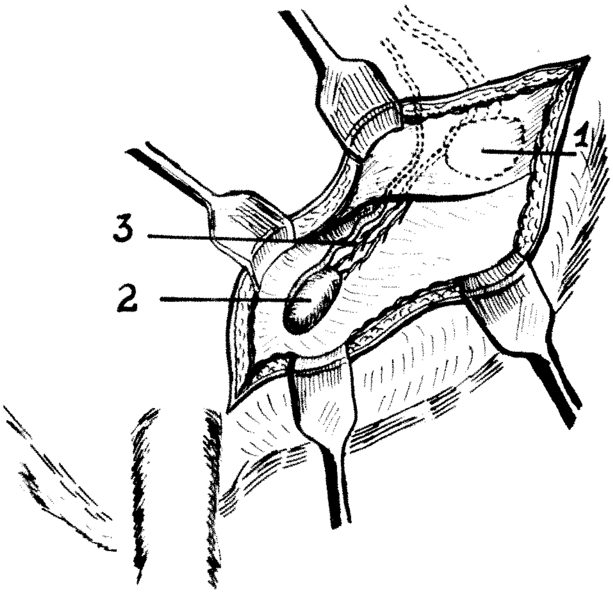

FIG. 2
The findings in the case described are: 1. The testis at the internal ring. 2 and 3. The epididymis and the spermatic duct descending into the scrotum; there is no connection between the first and the last two organs. (The sketch is very similar to that of Dean, A. L., *et al.* (1952) in "Failure of fusion of the testis and epididymis", *The British Journal of Urology*, **68**, 754-758.)

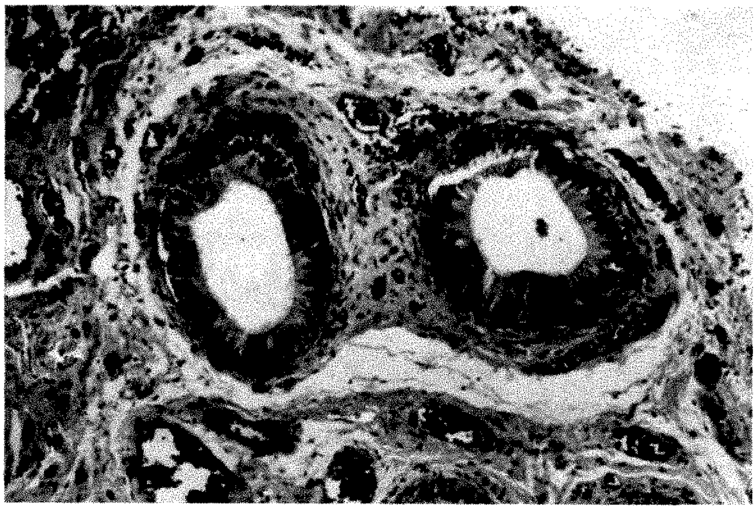

FIG. 3
The epididymis showing no abnormality.

(*a*) Complete absence of the testicle (anorchia) with the epididymis and the spermatic duct in the scrotum.
(*b*) Ectopic testis (abdominal or inguinal) with the epididymis and the spermatic duct in the scrotum.
(*c*) Ectopic testis and ectopic epididymis with a normally situated spermatic duct.
(*d*) Ectopy of all 3 elements: testicle, epididymis and spermatic duct.

In 1952 Dean *et al.* published a case showing bilateral malformation of the type *b*. These cases are extremely rare and the literature on the subject is scanty. It is considered that about 10 per cent of undescended testes are accompanied by such additional malformation, which makes its appearance approximately once in 250,000 male births.

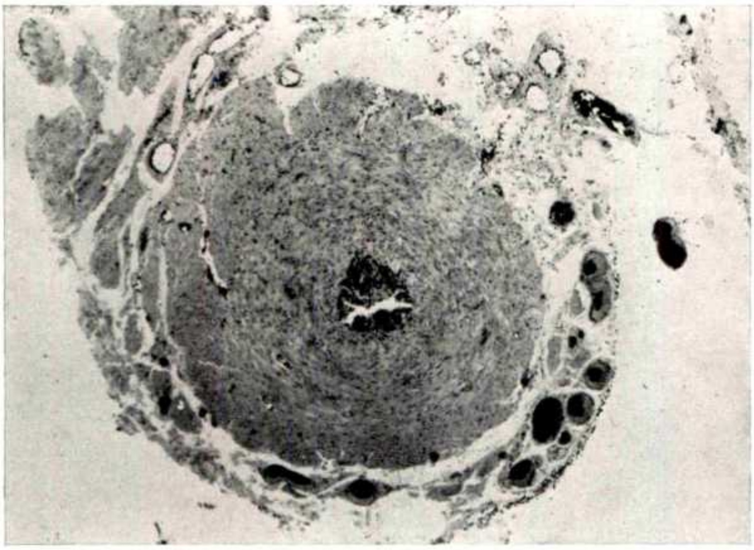

FIG. 4
The spermatic duct showing normal appearances.

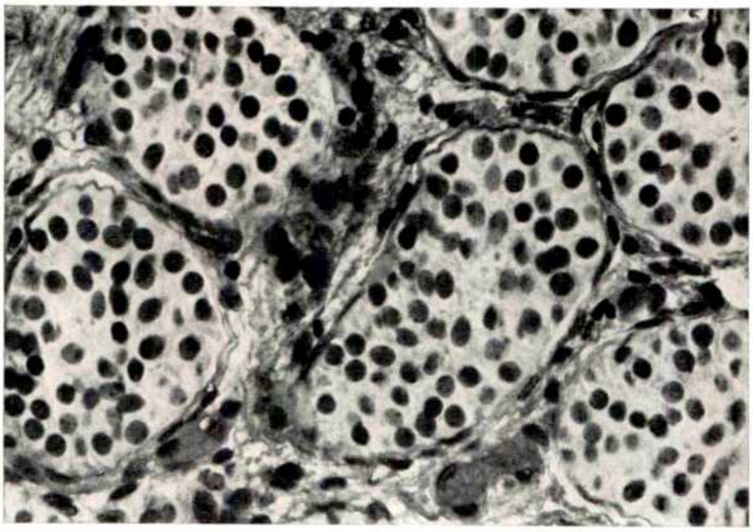

FIG. 5
Biopsy of the testis: normally developed tissue.

Case Report.—We present now one such case operated upon in our department: a 13-year-old Yemenite boy, born in Israel, was admitted with a left inguinal testis. There was nothing unusual in the history and he had never received hormonal treatment.

Physical Examination.—This showed a normally developed boy according to age, with visible pubic hair. The right testicle was normal in size and location. In the left side of the scrotum a small soft nodule 1 cm./1 cm.

was palpable. During coughing, another nodule, 2 cm./2 cm. could be felt at the upper end of the inguinal canal. At operation, after the aponeurosis of the external oblique had been opened, it was possible to identify the spermatic duct with its accompanying veins descending into the scrotum and entering a small yellowish nodule, which appeared to be the epididymis. Exploring the inguinal canal and close to the internal ring, the testis with the accompanying blood vessels was identified. There was no connection whatsoever between the two structures (Fig. 2). A small hernial sac of the congenital type was present. After excision of the sac, orchidopexy with biopsy of the testis was performed. Because of bleeding of the small vessels of the epididymis, it was excised. The post-operative course was uneventful.

Histological Examination.—The epididymis and the spermatic duct showed no abnormality (Figs. 3 and 4). Biopsy of the testis (Fig. 5) revealed a normally developed organ corresponding to the age of the patient. Most of the tubules showed non-active spermatogenic cells while some revealed an, as yet, undeveloped lumen.

SUMMARY

A rare case of congenital malformation of the testis is presented. A 13-year-old boy was operated upon for ectopic testis. At operation there was no connection between the testis, which was found at the internal ring of the inguinal canal, and the epididymis and spermatic duct, which were located in the scrotum. Orchidopexy was performed together with excision of the epididymis. The literature on the subject has been reviewed.

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NALIDIXIC ACID BY INTRAVENOUS INFUSION

A Report of 50 Cases

By G. Economou, M.D., R. Macis, F.I.M.L.T. and N. Ward-McQuaid, M.S., F.R.C.S.

Mansfield Hospitals

Nalidixic acid (Negram), a naphthyridine derivative, was described by Lesher *et al.* (1962). Since the drug was introduced in its oral form in Britain in 1963 its clinical uses have been described in over 120 papers including one from this hospital (Ward-McQuaid *et al.*, 1963). We have also used it intravesically (Conaghan and Ward-McQuaid, 1966).

Martin (1964) and Zinsser (1964) suggested that the sodium nalidixate preparation for intravenous use might be particularly useful in Proteus bacteræmia. By 1966 there were data in the files of the Sterling Winthrop Research Institute on 52 unpublished American case reports of patients with urinary infection or septicæmia of urogenital origin, the principle organism being Proteus, with some Klebsiella and coliform infections. Encouraged by these reports we started to use intravenous nalidixic acid in selected cases in 1967. We now report on the first 50 patients so treated.

CLINICAL TRIAL

Method.—Collection of specimens was by mid-stream unless a catheter was already in position, or a cystoscopy done. Standard Mast Laboratory sensitivity discs were used, ampicillin 25 μg., colistin 200 μg., gentamicin 10 μg., and nalidixic acid 30 μg.

The nalidixic acid was given by intravenous infusion from 1 to 4 days, 1 g. 8-hourly. The 10 ml. ampoules containing 10 per cent sodium nalidixate were diluted in at least 500 ml. of dextrose 4·25 per cent and 1·8 per cent saline, or 0·9 per cent saline, and followed by oral nalidixic acid, 1 g. every 4 hours for a total of 14 days nalidixic acid. The relevant reduced dose was used in children.

Infection of the urine was diagnosed by a positive culture with over 5 leucocytes per high-power field in the deposit, and a count of over 100,000 per ml. A cure was defined as a sterile urine 14 days after completion of the course. Check urine specimens were also examined at 3, 7 and 14 days after the course began.

Material.—The indications for giving nalidixic acid intravenously in the 50 patients are shown in Table I. There were 40 men and 10 women, their ages ranging from 2 to 86. All were known to have infected urines with organisms sensitive to nalidixic acid. Prostatectomy was done in 23 patients, retropubic in 17 and per-urethral in 6. A partial cystectomy was also done in 3 patients, in one for a vesico-colic fistula. Upper-urinary tract operations for stone and hydronephrosis were done in another 11 and a further patient had acute pyelonephritis with vomiting. In another group of 7 patients there was a Gram-negative septicæmia associated with urogenital sepsis and instrumentation. One of these had rigors with an impacted stone. There were 5 other patients who had difficult instrumentation, 4 having had previous rigors.

Treatment was started with nalidixic acid alone in 45 patients. Another drug was added because of chest complications in 3. Combined therapy was used in 5 from the outset, where there were also insensitive organisms (Table II).

The 60 infecting organisms in 50 patients were made up of Proteus and E. coli (23 each), Klebsiella (13) and one *Ps. aeruginosa*, with some mixed infections.

In 13 of the 50 patients organisms were sensitive to nalidixic acid but not to ampicillin, tetracycline or sulphonamides. In 2 the organisms were sensitive only to nalidixic acid of the usual drugs tested. The blood cultures in 5 of the 7 patients with clinical septicæmia grew Klebsiella (2), E. coli, Proteus and *Ps. aeruginosa*, this last not sensitive to nalidixic acid.

TABLE I

Diagnoses and Results in 50 Patients Treated with Intravenous Nalidixic Acid (Cures 14 Days after Course in Brackets)

Indications	Total	Antibacterial agents used		
		Nalidixic acid only	Combined *ab initio*	Combined later chest infection
Prostatectomy	23 (9)	20 (8)	0	0
Partial cystectomy	3 (0)	3	0	0
Renal operations	11 (9)	8 (7)	1	2 (2)
Pyelonephritis	1 (1)	1 (1)	0	0
Gram-negative septicæmia[1]	7 (3)	2 (1)	4 (2)	1
Instrumentation	5 (3)	5 (3)	0	0
Total	50 (25)	42 (21)	5 (2)	3 (2)

[1] Two patients in this group died.

TABLE II

Therapy Combined with Intravenous Nalidixic Acid from Outset (5 Patients)

Diagnosis	Organisms	Other drug combined with nalidixic acid	Results
Carcinoma of bladder, extravasation of urine, indwelling catheter	Klebsiella, mixed chest infection	Penicillin	Cure
Urethral stricture, indwelling catheter, septicæmia	Two Klebsiella	Colisitin	Resistant *Strep. faecalis* late elimination
Carcinoma of rectum indwelling catheter, septicæmia	E. coli, Proteus *Ps. aeruginosa*	Carbenicillin (later gentamicin)	Cure
Recurrent operation for staghorn renal calculus	Proteus, *Ps. aeruginosa*	Tetracycline	Cure
Diabetes, pneumonia, indwelling catheter, septicæmia	Coli, Klebsiella, mixed chest infection	Tetracycline	Died

RESULTS

In November and December 1970, 596 Gram-negative organisms were isolated in the Mansfield Group Laboratory from the first urines of each patient examined in this period (Table II). The overall sensitivity was ampicillin 61 per cent, nalidixic acid 84 per cent, colistin 70 per cent, gentamicin 96 per cent. The nalidixic acid/Klebsiella sensitivity is below the 84 per cent average of the previous 2 years (Pujari *et al.*, 1971) while the ampicillin/coli sensitivity is less, and ampicillin/Proteus sensitivity more.

Patients given Nalidixic Acid alone.—Of these 42 patients, 21 completed the 14-day course, first intravenously, then by mouth, and had a sterile urine 14 days later. Another 6 had clear urines at the end of the course, but a relapse of infection 14 days later with *Strep. faecalis* (3), coli (2) and Klebsiella. Resistance developed in 4 of the original organisms (Proteus (3), Klebsiella (1)).

TABLE III

Mansfield Area Laboratory—% Disc Sensitivity

596 Gram-negative Organisms, Nov.-Dec. 1970

	Total Orgs.	Incidence %	Ampicillin	Nalidixic acid	Colistin	Gentamicin
Esch.-coli	291	49	81	96	100	100
Proteus sp.	185	31	71	86	3	92
Klebs. sp.	95	16	0	65	99	96
Ps. aeruginosa	25	4	0	4	100	100
Total	596					
No. sensitive	Overall		365	498	416	577
% sensitive	Overall		61%	84%	70%	96%

Chest complications required the addition of another antibacterial agent in 3, with 2 cures. In 9 patients classed as failures the original organism was eliminated, but by a different resistant one (*Strep. faecalis* (8) Klebsiella (2), and Proteus (1)). Ultimately most of these patients had a sterile urine, either after further antibacterial agents or the healing passage of time.

Patients given Combined Therapy ab initio.—In 5 complicated cases nalidixic acid was used with another antibacterial agent from the beginning (Table II). In 3 a cure was obtained, in one the original organism was eliminated, but replaced by a resistant *Strep. faecalis*, later clear. One patient died.

Analysis of Results by Diagnosis and Operation (Table I)—Of the 23 patients who had a prostatectomy, 9 were cured by nalidixic acid alone, and the urine ultimately became sterile in all but one of the remainder. The 3 patients who had a partial cystectomy remained infected. The patient with pyelonephritis, and 7 with renal operations who received only nalidixic acid, were also cured. Two of the other renal cases were cured after another agent had been added for chest complications, and the fifth after combined therapy had been followed by a further antibacterial agent. None of these 45 patients had clinical evidence of bacteræmia while under treatment. Two of the patients with Gram-negative septicæmia died, both from terminal pneumonia. Three were cured by combined therapy from the beginning, and in the remaining 2 the infection was eventually eliminated.

Patients with Clinical Infection but Sterile Urine at Operation.—There were 4 other patients in whom the urine was thought to be infected because of previous reports and cystoscopic findings, but the urine specimen at operation proved to be normal. Of these 4 had a prostatectomy and one also a partial cystectomy, and the urine remained sterile.

Side Effects.—With this slow intravenous infusion there were no local effects. One drip ran for 3 days in the same vein. The only possible general reaction was transitory, and occurred

36 hours after the intravenous infusion had ceased, in a patient on both oral nalidixic acid for the urine infection and ampicillin for chest complications, both of which drugs had been given previously. It was probably a central nervous effect possibly due to sensitisation.

There is no evidence that the nalidixic acid had any ill effect on the two seriously ill patients with multiple pathology whose immediate cause of death was pneumonia. In one, the last patient in Table II, the nalidixic acid had stopped 24 hours before death. The other patient suffered from cirrhosis of the liver, bleeding œsophageal varices, retention of urine with severe urinary infection and had an indwelling catheter and clinical septicæmia. The urine had grown Proteus and Klebsiella, both sensitive only to nalidixic acid, colistin and gentamicin. The nalidixic acid was given for 3 days, and a combination of ampicillin and cloxacillin added later for his terminal pneumonia.

Contra-Indications to Intravenous Nalidixic Acid.—Obviously nalidixic acid must not be given in the very few patients who have had side effects previously. A drug history must always be taken, and precautions taken when any drugs are mixed in intravenous infusions, as stressed by Jacobs (1970) and a recent editorial in the *British Journal of Anæsthesia*, 1971. We know of two contra-indications to nalidixic acid. Epsilon amino-caproic acid (EACA) (Lawrence *et al.*, 1966) is still used in many patients having prostatectomy, but this produces a milky appearance with nalidixic acid. There is also one report from elsewhere of precipitation with a 5 per cent dextrose solution, which should also be avoided.

Watson (1971) added 10 ml. of nalidixic acid injection (100 mg./ml.) to 500 ml. 5 per cent glucose solution. No immediate precipitate formed and the solution remained clear for at least a week. After approximately 3 weeks white needle crystals were observed in the solution. The crystals were filtered off and identified by infra-red spectroscopy as nalidixic acid. The pH of the solution was 7·5. Although no sample of the precipitate observed in the reported incident was available it is reasonable to assume that it was nalidixic acid.

In view of these findings the manufacturers recommend dilution of 1 g. of sodium nalidixate by at least 500 ml. of normal saline.

DISCUSSION

Review of Literature.—There have been few published reports. The two principal papers are by Zinsser (1970) who treated 25 patients with 28 courses, 12 with nalidixic acid alone; and Zinsser and Doenecke (1970). Zinsser used nalidixic acid when this was the only drug to which the organism was sensitive on blood culture, or when existing therapy had failed to control the situation. He had good or excellent results in 7 of the 12 in which nalidixic acid was used alone, in 5 of 7 in which it was used with colistin and 3 of 6 when used with chloramphenicol.

Zinsser and Doenecke (1970) also described 25 cases of intravenous nalidixic acid administered to 23 patients with urogenital septicæmia or threatened septicæmia without evident side effects. Overall results were excellent in 6, good in 9, moderate in 6, and poor in 4.

Zinsser and Doenecke (1970) found the mean blood level " ranged between 30 and 50 μg./ml., a level high enough to control 70 per cent of our most resistant cases of Aerobacter-Klebsiella Gram-negative sepsis ". Recent biological assay work, in the files of Winthrop Laboratories Research Institute, as yet unpublished, has shown that the mean plasma level of biologically active nalidixic acid in 7 subjects, following a 1 g. oral dose, was 19 μg./ml. at 2 hours. The level fell rapidly after this, suggesting the value of giving an infusion and maintaining a high level of the drug in seriously ill patients.

In the 42 patients in our present series treated only with nalidixic acid, results were excellent in 21 whose urine was sterile 14 days after treatment had finished, and good in the 6 where the urine was clear at the end of treatment but had relapsed 2 weeks later. In the 8 patients who had combined therapy there were excellent results in 4. There were 2 deaths in the 7 in the septicæmia group. In the 50 patients results were excellent in 25 and good in another 6.

In a symposium (McAllister and Percival, 1971) on clinical and bacteriological aspects of urinary tract infections it was reported that 93 per cent of the three important Gram-negative organisms, E. coli, Proteus and Klebsiella are sensitive to nalidixic acid.

In the absence of relevant urine sensitivity results nalidixic acid is likely to be more effective, at least in our hospital, than colistin and also ampicillin, even when the relatively few Gram-positive organisms, some of which at least are contaminants or of low virulence, are included. Sulphonamides and tetracycline are less effective and the promising sulphamethoxazole/trimethoprim preparations cannot be given parenterally. Kanamycin and gentamicin are usually reserved for the most severe infections and we have, as yet, no great experience with the cephalosporins by injection.

Importance of Infection.—Blood stream infection after prostatectomy may occur with a previously sterile urine, but is much more common with an infected urine (Last, Harbison and March, 1966). It may also occur without symptoms (Barrington and Wright, 1930). Appropriate antibacterial cover in infected patients reduces the higher incidence and duration of bacteræmia and subsequent mortality from pyelonephritis and septicæmia (Marshall, 1967; Ives, Brown, Jones, Marshall and Campbell, 1971). Sachdev, Chitkara, Marya, Chhanra and Singh (1968) found Proteus the most common organism in bacteræmia.

Mitchell, Slade and Linton (1962) discussed bacteræmia after instrumentation, and considered that *Strep. faecalis* was of lower virulence than the usual urinary organisms, but almost more resistant to chlorhexidine. This organism is sometimes only a urinary contaminant, or it may occur with an underlying cause when the original infecting organism, usually Gram-negative, has been eliminated as in half the failures in the present series. If found before prostatectomy or instrumentation it should be treated and it is, of course, of particular importance in patients with cardiac valvular diseases.

Opinions differ as to whether or not it is necessary or desirable to attempt to eradicate a *Strep. faecalis* infection in the second week after prostatectomy, when instrumentation is over. If this is attempted then the question of completing the fortnight's course of nalidixic acid in addition to the other antibacterial agents must be considered (except in the case of nitrofurantoin) in an effort to prevent a relapse of the original infection. A fortnight's course seems desirable because relapse is common at this stage with the prostatic bed only starting to heal. Even after a 2 weeks' course 6 of the 27 patients with a sterile urine had relapsed 2 weeks later.

Ives *et al.* (1971) found bacteræmia in 12 per cent of urological patients, and more often in those undergoing prostatic surgery than in all other groups together. Bacteræmia was also found in patients having multiple urethral instrumentation and even transrectal prostatic biopsy. There were no cases in this series in upper urinary tract operations. In patients with infected urine undergoing renal surgery for stone or hydronephrosis, however, antibacterial agents are used rather to sterilise the urine soon after operation, and discourage any recurrence of infection or stones. We had one patient with rigors and bacteræmia associated with an impacted stone.

Indications for Intravenous Nalidixic Acid.—When the urine is infected before prostatectomy, or renal operation, it is common practice to cover the operation with the appropriate antibacterial agent. These patients usually have an intravenous drip infusion for the first one or two days, and this is the most comfortable and efficient route for drug administration until the patient is swallowing readily. Patients with vomiting from pyelonephritis and those with Gram-negative septicæmia also require an intravenous infusion. Tetracycline and ampicillin are frequently given in this way and the intravenous preparation of nalidixic acid will also prove useful. Intravenous nitrofurantoin is not available in this country, but Miller, Scott and Scott (1964) in the States found a reduction in complications after prostatectomy with infected urine when nitrofurantoin was given intravenously.

In patients with grave Gram-negative septicæmia of urogenital origin one would use gentamicin, kanamycin or chloramphenicol. In a life-threatening situation which often has to be treated on the " best guess " principle, a penicillinase-resistant penicillin such as cloxacillin, or a cephalosporin, may be combined with gentamicin for full cover (Brumfitt and Percival, 1971). *Ps. aeruginosa* infections may require colistin or carbenicillin.

Zinsser and Doenecke (1970) considered the blood levels with intravenous nalidixic acid, although variable, to be high enough to affect the more resistant organism. The rapid excretion of nalidixic acid by the kidney may make it safer in renal failure, and certainly gives a high concentration in the urine and site of origin of the infection. Stamey *et al.* (1969), after oral nalidixic acid, found the serum levels of both nalidixic acid and hydroxynalidixic acid to be remarkably high in relation to the concentration required to kill most Gram-negative pathogens. These serum levels might be clinically useful in patients with tissue infection due to Gram-negative infection. In renal failure urinary levels were bactericidal without accummulation of biologically active drug in the serum. They considered nalidixic acid to be particularly valuable in Klebsiella and indole-positive Proteus urinary infection.

It would seem safe and reasonable to give nalidixic acid intravenously when it is the drug of choice and when it cannot be given by mouth. In complicated cases combined therapy is given as indicated.

SUMMARY

Nalidixic acid was given by intravenous infusion to 50 patients with infected urine; 1 g. of the sodium salt was diluted with at least 500 ml. saline and given 3 times a day for 1-4 days. There were no side effects. The full 14-day course was then completed by mouth. Results were excellent in half the patients, with sterile urine 14 days after completion of the course.

Our thanks are due to Professor C. P. Beattie in whose Mansfield Area laboratory the bacteriological work was done, and to Mr Alexander Marshall, F.R.C.S., for his interest.

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NEWS FROM HOME AND OVERSEAS

INSTITUTE OF UROLOGY (UNIVERSITY OF LONDON)

The British Postgraduate Medical Federation have invited the postgraduate Institutes to arrange a series of 2-week Advanced Training Courses for N.H.S. Consultants, Senior Registrars and certain Registrars. The first of these courses at the Institute of Urology will take place between 27th September and 7th October, and will be on " The Surgery of the Urethra ". Further details may be obtained from the Secretary, Institute of Urology, 172 Shaftesbury Avenue, London, W.C.2.

ABSTRACTS FROM CURRENT UROLOGICAL LITERATURE

Acta Urologica Japonica

By D. I. ROBERTS

"So-called Essential Renal Hematuria and the Fibrinolytic Enzyme System." H. MANABE. (1971, **17**, 314-329.)—15 patients with essential renal bleeding were studied for fibrinolytic enzyme activity. The fibrinolytic system in the blood was inactive in controls but active in all patients with haematuria. The levels of urinary activator were higher in the patients than in controls. This work was carried out at Chiba University.

"The Mechanism of the Transport of Urine after Urine Diversion to an Ileal Conduit." T. YAMAUCHI. (1971, **17**, 376-393.)—17 patients with urinary conduit were studied at Nagoya. The frequency of systolic movements at the uretero-pelvic junction was within normal limits. Ureteric reflux was demonstrated in 53% of cases. Excretory cinefluorography of the ileal conduit showed weak, non-propulsive movements, but stasis of urine was never demonstrated.

"Studies on Water, Electrolytes and Acid-base balance before and after Urological Surgery." T. KOMIYA. (1971, **17**, 3-32.)—At Yamaguchi University Medical School, biochemical studies of blood and urine were made before and after urological surgery in order to establish rational methods of fluid replacement. Postoperatively there was a transient elevation of serum NPN and a decrease in the urinary excretion of sodium. When Ringer lactate was administered during operation and more than 100 mEq sodium per day given postoperatively, biochemical changes were kept to a minimum.

"Experimental Studies of Essential Hemospermia with Special Reference to the Fibrinolytic Activity." S. KOSAKA. (1971, **17**, 253-276.)—In this detailed article from Kanazawa University, a review of the literature on haematospermia is made. The condition can be classified as "organic" when there is an obvious cause or "essential" when the cause is obscure. It has been found that cases of essential haematospermia, the fibrinolytic activity of the seminal fluid is high and it has been suggested that this is due to an allergic reaction in the vesicles. Using rabbits, the author has attempted to support this hypothesis. He consistently produced an allergic reaction in the vesicles with submucous oedema and petechial haemorrhages.

"Study on Arterio-Venous Shunt for Hemodialysis. 11." J. KAWAMURA and 4 other authors. (1971, **17**, 33-46.)—This study from Kyoto covers 26 patients treated for 2 years by intermittent haemodialysis. All patients were equipped with a Quinton-Scribner shunt in either the arm or the leg. Shunt survival on the arterial side was 14 to 17 months and on the venous side 10 to 12 months. Complications were more common on the venous side and were associated with clotting, mechanical deficiency, infection and bleeding in that order of frequency. Angiography of the shunt was used as a preliminary to recannulation and was found helpful.

"Hemodialysis with Gambro Filter. (Disposable Parallel Flow Dialyser.)" J. KAWAMURA and 5 other authors. (1971, **17**, 100-112.)—At Kyoto University Hospital, the Gambro filter was used for haemodialysis on 10 patients who had been on regular intermittent dialysis with a Kiil dialyser for 1 year. At a blood flow of 200 mls. per minute, the Gambro filter gave dialysances of urea, nitrogen and creatinine that were 10% better than the Kiil. In order to extract the same amount of water, negative pressure on the dialysis fluid had to be doubled in the Gambro filter as compared with the Kiil. The Gambro filter is compact, ready to use and only needs a small volume of priming fluid.

The Journal of the American Medical Association

By D. T. H. PAINE

"The Ninth Report of the Human Renal Transplant Registry." Prepared by the Advisory Committee to the Renal Transplant Registry. B. A. BARNES, J. J. BERGAN, W. E. BRAUN, C. L. HAMPERS, D. E. KAYHOE, F. K. MERKEL, S. L. KOUNTZ, M. R. MICKEY, A. L. RUBIN, R. L. SIMMONS, L. E. STEVENS. (1972, **220**, 253-260.)—The headquarters at the American College in Chicago, report on data from 5,952 kidney transplants in 5,432 patients. This information includes all cases reported to the Registry since 1953. All those who have to answer questions on the problems of survival, success, rejection, etc., of renal transplantation should have this report to hand. It is confirmed that there has been very little change in patient survival and duration of function of transplants performed during the last 4 years. The incidence of cases treated lists glomerulonephritis (60%) pyelonephritis (16%) polycystic disease (5%). Cadaver kidneys are being increasingly used, rather than living donors. At this time, patient survival in those receiving a familial graft approaches 90% at 1 year and 75% at 2 years. For cadaver grafts, the figures are 70% at 1 year and 60% at 2 years. The presentation has easily read and understood graphs.

"Occlusion of the Renal Artery Secondary to Acute or Remote Trauma." S. H. CORNELL, D. A. REASA, and D. A. CULP. (1972, **219**, 1754-1755.)—At the University of Iowa Hospitals 5 patients were seen with traumatic occlusion of the renal artery in 3 years. 4 were of early and 1 of remote onset. The authors suggest that where a traumatised kidney is not visualised on the I.V.P. and shows no distortion on retrograde pyelography, arteriography should be performed. Incomplete obstructions may be remediable.

"Preservation of Human Cadaver Kidneys for Transplantation." R. E. MCCABE, JR., and H. F. FITZPATRICK. (1972, **219**, 1056-1059.)—10 hospitals in New York City co-operated in a regional organ procurement programme. Tissue typing of the recipient pool of more than 200 was performed by the New York Blood Center. In 1 year, 30 kidneys were provided. A Belzer organ perfusion apparatus was used. 20 kidneys were selected for tranplantation at

5 different centres. Short term graft survival approached 85%.

"**Lymphoma, A Complication of Renal Allotransplantation in Man.**" J. C. Pierce, M. E. Madge, M. D. M. Lee, and D. M. Hume. (1972, **219,** 1593-1957.)—Reporting from the Virginia Commonwealth University the authors describe 3 cases of reticulum cell sarcoma occurring in a series of 151 renal transplant recipients over a period of 438 patient survival years, an incidence of 0·7% per year. They state that this is more than 100 time greater than that in the general population. They suggest that the immunosuppressive therapy in the presence of the foreign transplant was responsible.

"**Transient Reappearance of Sperm After Vasectomy.**" S. Marshall, and R. P. Lyon. (1972, **219,** 1753-1754.)—Every fourth ejaculate was examined in 400 post-vasectomy patients. In 8 patients sperm reappeared occasionally. They describe 1 case where 5-6 motile sperms per high power field were seen 4 months after vasectomy. This patient's wife was pregnant. Azoospermia occurred 6 months after vasectomy.

"**Splenectomy in Renal Transplantation.**" J. E. Woods, J. S. Deweerd, W. J. Johnson and C. F. Anderson. (1971, **218,** 1430-1431.)—These workers have looked into the effect of preoperative splenectomy on the incidence of leukopenia after transplantation in patients receiving azathioprine. It would appear that preoperative splenectomy increases the tolerance of patients to azathioprine in respect to leukopenia.

"**Human Renal Function Following Methoxyflurane Anaesthesia.**" R. B. Merkle, D. McDonald, J. Waldman, G. D. Maynard, J. Petit, J. Fleming and W. J. Murray. (1971, **218,** 841-844.)—The recent realization that methoxyflurane anaesthesia may create changes in renal function prompted these investigators to examine 25 patients receiving this drug, and 25 receiving halothane, all of whom were undergoing surgical repair of retinal detachment, an operation not usually accompanied by hypotension, blood loss, etc. They found a significant rise in mean creatinine level and a fall in the mean urine osmolality in those receiving methoxyflurane. The halothane recipients showed no such changes.

"**National Transplant Communications Network.**" P. I. Terasaki, G. Wilkinson, and J. McClelland. (1971, **218,** 1674-1678.)—These workers describe the present network for pooling information for cadaver kidney transplant-sharing in the United States of America and Canada. Although the information given is incomplete to my own knowledge in regard to Canada, the article points out the advantages of a large pool of recipients. The expected rise in the number of group O waiting recipients is confirmed. This is due to the use of type O kidneys for type A or B recipients. At the time of reporting, there was a total of 864 waiting recipients from 61 transplant centres with information on the computerized file. At that time a total of 215 kidneys had been exchanged on the network.

"**Renal Pelvis Tumours.**" H. Grabstald, W. F. Whitmore and M. R. Melamed. (1971, **218,** 845-854.)—A new classification for renal pelvic tumours is suggested. Group 1: Histologically Benign Papilloma (*a*) without other tumours in bladder or ureters, (*b*) with such other tumours. Group 2: Low Stage Carcinoma with no, or only questionable or microfocal invasion or papilloma with carcinoma-in-situ either within the papilloma or elsewhere in the renal pelvic mucosa. (*a*) and (*b*) as above. Group 3: High Stage Carcinoma confined to the kidney, (*a*); (*b*) as above. The prognosis is excellent for patients in Group 1 or Group 2. It is also good for patients with invasive carcinoma confined to the kidney (Group 3). In about half of the cases there were associated tumours elsewhere in the uro-epithelium and the prognosis may be determined by these tumours. Bladder growths which developed usually did so within 3 years. Total nephro-ureterectomy remains the treatment of choice. Local resection or partial nephrectomy is recommended for bilateral pelvic tumours. The above conclusions are based on the study of 70 patients.

Annals of Surgery

By A. R. C. Higham

"**Preoperative Extracorporeal Irradiation of the Blood as Adjunctive Immunosuppression in Human Renal Transplantation.**" B. Persson, B. Rosengren, R. Olander, S-E Bergentz, L-E Gelin and B. Hood. (1971, **174,** 802-810.)—From the University of Goteborg, Sweden. 27 patients received a total of at least 9,000 rads of ECIB at 5 or more treatments before transplantation. These were compared with 97 patients who did not receive any ECIB. During the first 4 months there was a significant decrease in the incidence of all recognisable rejection episodes in the ECIB group—and there seemed to be a prolongation of 30% in the graft survival time.

"**Subtotal Parathyroidectomy in Chronic Renal Failure.**" R. E. Wilson, C. L. Hampers, J. W. Johnson and J. P. Merrill. (1971, **174,** 640-651.)—A series of 28 patients undergoing subtotal parathyroidectomy for renal osteodystrophy after receiving renal allografts was studied at the Harvard Medical School. 26 had chief cell hyperplasia: 1 a parathyroid adenoma and 1 multiple myeloma. With the exception of the latter, all did well.

"**Concurrence of Hypernephroma and Hypercalcemia.**" M. M. Warren, D. C. Utz and P. P. Kelatis. (1971, **174,** 863-865.)—To determine the incidence of hypercalcaemia with hypernephroma, 400 consecutive cases of hypernephroma were studied at the Mayo Clinic. 4% had hypercalcaemia preoperatively.

"**Hypoplastic Inferior Vena Cava with Aplasia of the Right Kidney and Adrenal Gland.**" J. M. Provost, C. M. Hoffman, J. F. Ryan and D. H. Vines. (1971, **174,** 843-847.)—From the United States Army Hospital, Fort Ord, California. An unusual case with the above abnormalities is reported. The patient was 20 years old, and presented with dilated veins on the abdominal wall.

"**An Unusually Large Gas-Containing Bladder.**" L. E. Fetterman. (1972, **45,** 67-69.)—From Mobile, Alabama. A 75-year-old male, non-diabetic, presented with marked abdominal distension. At operation 2 gallons of urine were removed: there was a 300-gram prostate, and infection of the bladder with a gas-producing organism.

"**Intrarenal Mycotic Aneurysm Detected Angiographically.**" R. E. Clark, T. O. McNamara and A. J. Palubinskas. (1972, **45**, 66-67.)—From the University of California School of Medicine, San Francisco. The patient, a 20-year-old man, had multiple blood cultures which grew *Staph. aureus*. The ^{203}Hg-chlormerodrin renal scintigraph showed a 3 mm. non-labelling area in the lower pole of the right kidney. Selective R. renal angiography showed non-specific saccular dilatation.

"**Immunosuppression, Liver Injury, and Hepatitis in Renal, Hepatic and Cardiac Homograft Recipients.**" M. Torisu, T. Tokoyama, H. Anemiya, W. Palmer, C. G. Halgrimson, C. W. Putnam and T. E. Starzl. (1971, **174**, 620-634.)—From the Univeristy of Colorado School of Medicine. The hepatitis associated with an Australian (Au) antigen has been found by precipitation detection methods in the sera of almost ¼ of a group of 89 chronic survivors after renal, hepatic or cardiac transplantation. However, the frequency of derangements in hepatic function was essentially the same with or without Au antigen being detected. A patient dying of chronic aggressive hepatitis, Au positive, was submitted to liver replacement, and then treated with azothioprine, prednisone and heterologous horse antilymphocyte globulin. Within minutes of removal of the liver the Au antigen disappeared from the serum suggesting that the native liver had been its primary source. The antigen returned many weeks later just before the onset of a moderately severe bout of hepatitis affecting the homograft.

"**Relative Importance of Cellular and Humoral Immunity in Human Renal Transplantation.**" J. C. McDonald, M. D. Kappellman, B. H. McCracken and M. O. Hornung. (1971, **174**, 602-615.)—From Tulane Univeristy School of Medicine and the Charity Hospital of Louisiana. 42 cell-inhibition assays were performed in 26 human recipients from living related donors at 22 days to 34 months postoperatively to determine the presence or absence of immune lymphocytes and specific serum-blocking activity. 85% of lymphocytes tested in the first 12 months postoperatively inhibited donor fibroblast growth *in vitro*. Within the interval of 1-12 months after transplantation this lymphocyte-mediated inhibition was frequently blocked by the patient's serum, and there was a good correlation between the blocking activity and a favourable clinical course. After 12 months 85% of the lymphocytes were either non-reactive or specifically blocked by recipient serum.

"**Renal Transplantation in Infants and Children.**" J. S. Najarian, R. L. Simmons, M. B. Tallent, C. M. Kjellstrand, T. J. Buselmeir, R. L. Vernon and A. F. Michael. (1971, **174**, 583-600.)—The outstanding features in this report from the University of Minnesota are: (1) 56 children aged 1-16 and 2 infants have received renal transplants since 1963. (2) Of 24 patients transplanted between 1963 and 1967, 50% of recipients of related kidneys are well with their 1st transplant and 15% are well with their 2nd transplant. 16% of recipients of cadaveric kidneys are well with their 1st kidneys and 16% are well with their 2nd kidneys. (3) Of 24 children aged 1-16 transplanted with kidneys from related donors since 1968 only 1 has died, and only 1 has lost his kidney. Of 6 children aged 1-16 transplanted with cadaveric donors since 1968 all are alive and 5 have good renal function. (4) Patients with obstructive uropathy do as well as patients with nephritis if refluxing ureters have been removed. (5) Patients with steroid-resistant nephrotic syndromes seem to have poor prognoses and the disease may recur in the transplants. Prolonged dialysis may reduce this tendency. (6) General growth after transplantation parallels the normal growth of children, but "catch-up" growth rarely occurs. (7) Early post-transplant hypertension is a problem which requires vigorous measures to avoid central nervous system changes.

"**Viral Syndromes and Renal Homograft Rejection.**" D. S. David, S. J. Millian, J. C. Whitsell, G. Schwartz, R. R. Riggio, K. H. Stenzel and A. L. Rubin. (1972, **175**, 257-259.)—From the New York Hospital-Cornell Medical Center. 3 recipients of renal transplants had 6 episodes of viral syndromes consisting of upper respiratory or gastro-intestinal symptoms. Within a period of a few days to 1 month these episodes were followed by a marked drop in renal function which in most instances resembled an acute rejection. The authors suggest that in some patients there may be a cause and effect relationship between viral infections and renal transplant rejection.

Archivos Espanoles De Urologia

By C. I. C. Charlton

"**Spontaneous Peri-renal Haematoma.**" L. A. Cotado and P. M. Medina. (1971, **24**, 173-184.)—The authors classify spontaneous peri-renal haematoma into 3 groups: those cases in which there is an abnormal kidney associated with the haematoma; those in which the bleeding is due to an extra-renal lesion (aneurysm, supra-renal disease or blood dyscrasias); and finally those cases in which no cause for the haematoma is found. They review the literature, and state that the clinical features associated with this condition are the presence of lumbar pain, the signs of haemorrhagic shock, and the presence of a retro-peritoneal mass. In addition, a fever is commonly present, and discolouration due to the bruising which may extend to the scrotum. On plain X-ray, the lateral border of the psoas shadow may be absent, and on IVP, the kidney is displaced (if the bleeding is of extra-renal origin). They describe a case in which the diagnosis was made preoperatively, but no cause for the haematoma was found.

"**Right Sided Ovarian Vein Syndrome.**" A. G. Collar and J. M. A. Boix. (1971, **24**, 315-330.)—The authors studied the so-called right ovarian vein syndrome, which is caused by the compression of the ureter at the level of its crossing the common iliac artery by a varicose ovarian vein. The diagnosis is made on the pyelogram, which shows the following features: dilatation of the pelvis, tortuous ureter, "spindling" of the ureter, "notch-like" vascular impression at the level of the iliac artery, and disparity in size between the dilated upper ureter and the normal sized pelvic ureter. The authors had 10 cases of women who presented with symptoms of urinary infection or obstruction. 6 were managed with drugs; in 4 cases operation was undertaken. They found the ovarian vein to be varicose and compressing the ureter against the iliac artery. Following this procedure there was no change in the radiological picture, but the patients were improved symptomatically.

British Journal of Radiology

By A. R. C. Higham

"An Unusual Manifestation of Ureterocoele." I. W. McCall. (1972, **45**, 218-219.)—A case is described of bilateral ureterocoeles lying within vesical diverticula. A review of the literature revealed 1 case where a large simple ureterocoele was located in a vesical diverticulum.

Journal de Chirurgie

By Geoffrey Parker

"A Personal Series of Seven Cases of Ruptured Testicle." J-C. Masson, J. Doremieux and Cl. Bollack. (1971, **102**, 323-330.)—All the cases were due either to accidents at football or in the course of a street fight. All were operated on within a matter of hours, a remarkable feature of the series being that in every case it was found possible to conserve at least part of the damaged testicle and to suture the tunica albuginea. Some of these patients did not come to hospital for a follow-up, but of those who did, the majority had adequate, though in some cases, reduced sperm counts. A total of 80 cases is reported from the literature, of which 2 were bilateral. For reasons which are not explicable the lesion is 3 times more common on the right side than the left. Early operation is strongly advocated in all cases. 35 references are taken from the world literature.

"A Report of Two Cases of Renal Neoplasia Associated with Renal Arteriovenous Fistulae." J-C Masson, A. Woessner, J. Tonoio and Cl. Bollack. (1971, **102**, 585-592.)—This paper is from the Urological Department of the Central University Hospital, Strasbourg. 127 of these cases, either congenital or acquired, have been found in the literature, of which the paper by Vaysse and his colleagues reporting 114 cases in 1970 in the same journal is the most important contribution to the subject. The 1st case here reported, who incidentally had noticed the recent occurrence of a varicocele on the left side, was admitted on account of clot retention of urine. A renal arteriogram demonstrated not only a centrally placed neoplasm, but also an arteriovenous fistula. A transperitoneal nephrectomy was successfully carried out, but both pulmonary and vertebral metastasis were noted. The 2nd case presented with extensive pulmonary metastases and the renal neoplasm, and arteriovenous fistula were discovered at routine arteriography. At operation for removal of the left kidney hepatic deposits were also noted but no explanation is offered for the fact that the general condition of the patient 3 months after operation was considerably improved. 17 closely similar cases are noted in the literature, and it would seem that the prognosis is particularly bad on account of the rapid dissemination facilitated by the presence of the vascular fistula.

"Embolism of the Renal Artery." M. Lacombe. (1971, **102**, 561-570.)—This paper from the Surgical Clinic of the Beauyon Hospital, Clichy, reports a rare cause of anuria being usually diagnosed only at autopsy. 3 cases are described, 2 of them being operated on successfully. In all 3 cases the other kidney was already functionless on account of pre-existing disease such as tuberculosis or pyonephrosis. The diagnosis of renal arterial block should suggest itself in cases of anuria associated with flank pain where it is known that there is also cardiac or atheromatous lesion particularly affecting the aorta. Surgery was preceded by some hours of haemodialysis and all 3 cases were totally anuric when they came to operation. Successful surgery in 2 cases consisted in removal of the renal arterial embolus; in 1 case a saphenous patch graft was necessary for satisfactory closure of the artery. Both ureteral catheterisation and aortography are essential for diagnosis, and the author is of the opinion that surgery is always worthwhile, however long the period of anuria may have been. Less than 40 cases are recorded in the literature.

Deutsche Medizinische Wochenschrift

By John Grieve

"Prepubertal Testicular Growth in Normal Boys and those with Brain Damage." F. Städtler and R. Hartmann. (1972, **97**, 104-109.)—Histological and histometric examination was done on the testes from 40 boys aged 1-10 who had died from accident or acute disease. These showed over the 10 years progressive development of the gonads with increases in testicular weight, tubular diameter and in the spermatogonia count. In contrast more than half of 32 children with brain damage showed diminished testicular growth, reduced tubule diameter and a reduced spermatogonia count. In 7 of the brain damage group normal progressive development to complete spermatogenesis was seen. The authors suggest that in early childhood there is increasing hypothalamic/hypophyseal control of testicular growth.

La Nouvelle Presse Medicale

By John Grieve

"Twelve Cases of Renal Atrophy due to Reflux." L. Boccon-Gibod, P. Gallian and L. Boccon-Gibot. (1972, **1**, 507-510.)—Among 12 kidneys removed for atrophy believed due to reflux, 6 showed renal dysplasia, 5 segmental renal hypoplasia and only 1 chronic pylonephritis. The authors suggest that true renal atrophy in association with reflux is very much less common than atrophy associated with congenital anomalies.

Surgery, Gynaecology and Obstetrics

By Thomas Moore

"The bacteriology of Ileal Conduit Urine in Man." P. D. Guinan, R. H. Moore, E. Neter, and G. P. Murphy. (1972, **134**, 78-82.)—At the Roswell Park Memorial Institute, New York State, the authors have studied the urines collected from 90 ileal conduits. 4 were palliative procedures only and 86 were associated with radical cystectomy. 56% of the preoperative bladder urines were infected while 74% of the ileal conduit urines were infected. In the precystectomy urines, proteus, E. coli and pseudomonas were the predominant organisms. In the ileal conduit urines, proteus was the most prominent. There was no correlation between the ileal conduit bacteriology and the sugar or protein content of the urine. In no case was there a large residual urine in the conduit. Recurrent proteus infection was often associated with the formation of recurrent calculi and also with renal dysfunction. Every effort should be made to rid the conduit of these organisms by antibacterial treatment and acidification of the urine.

"**Combination Chemotherapy in the Treatment of Germ Cell Tumours containing Choriocarcinoma in Males and Females.**" D. P. GOLDSTEIN and J. PIRO. (1972, **134**, 61-66.)—From the Peter Bent Brigham and associate hospitals in Boston, the authors report their results in 8 males and 2 females suffering from testicular and ovarian tumours containing trophoblastic elements and 1 similar retroperitoneal extragonadal tumour. They lay stress on the value of urinary gonadotrophin assays in the follow up after radical surgical extirpation and the control of recurrence by triple chemotherapy. This consisted of methotrexate, between 15 and 25 mgs per day, actinomycin D, between 500 and 750 micrograms per day, and cyclophosphamide, between 150 and 250 mgs per day. The drugs were administered intravenously for 5 consecutive days and these courses were repeated every 10 days to 6 weeks, depending upon the degree of marrow depression and systemic toxemia. The total number of courses administered ranged between 1 and 9. 4 male and 1 female patients have had a sustained remission without evidence of recurrent disease. The tumours consisting of pure choriocarcinoma appeared to respond better than those with mixed cell types.

"**The Renal Hemodynamic and Functional Effects of External Counterpressure.**" J. H. SHENASKY II, and J. Y. GILLENWATER. (1972, **134**, 253-258.)—In the University of Virginia School of Medicine, Charlottesville, the authors have carried out experiments on mongrel dogs. External abdominal pressure of 30 mms. of mercury was applied for 4 hours. Approximately 80% of the pressure was transmitted to the retroperitoneal space. A marked fall in cardiac output and renal perfusion was recorded, with resulting decrease in urinary output and an increase of sodium and water reabsorption. Kidney function did not return quite to normal after the pressure was relieved.

"**Landmarks in Clinical Renal Transplantations.**" C. G. GROTH. (1972, **134**, 323-328.)—The author, from the Department of Surgery, at the Karolinska Institute, Stockholm has produced a historical account of renal transplantation, with a very good, complete bibliography.

"**Alteration in Renal Metabolism occurring in Ureteral Obstruction in Vivo.**" J. F. STECKER, JR., M.D., E. D. VAUGHAN, JR., and J. Y. GILLENWATER. (1971, **133**, 846-848.)—Experiments carried out on mongrel dogs in Charlottesville, Virginia, by the authors, have shown that oxygen consumption and carbon dioxide production in the kidney were decreased in both acute complete and prolonged partial unilateral ureteral obstruction. Because the oxygen consumption was decreased relatively more than the CO_2 production, the respiratory quotient rose. The authors believe these changes were due to a decreased tubular reabsorption of sodium, so that less oxygen was used, and from an increase in anaerobic glycolysis and anaerobic decarboxylation reactions in the renal cortex.

"**Daniel's Technique for a Simplified Ileal Conduit.**" E. SHOCKET. (1971, **133**, 853-854.)—From the University of Miami, Florida, the author describes the technique which avoids freeing a loop of ileum with its fan of mesentery. An inverted U-shaped loop of mobile ileum, at least 12 inches from the ileocaecal junction, is measured, so that it reaches the abdominal surface easily. The distal limb of the loop is freed along its mesenteric border and removed. The mesentery proper is not incised. The proximal end is divided and if necessary for further mobility, a further piece of bowel can be removed, preserving the mesentery. Intestinal continuity is re-established, the conduit fashioned by closing its proximal end, and anastomosing the ureters separately to it and forming an ileal spout in the usual way. The method is said to be quicker, easier and safer than the more orthodox procedure.

"**The Effect of Chlorpromazine on Renal Function and Blood Pressure.**" E. L. HANSON, R. H. CLAUSS, B. SCHNEIDERMAN and E. S. BREED. (1971, **133**, 565-576.)—The authors have studied the effects of small intravenous doses of chlorpromazine, on the arterial and central venous pressures and on the renal function of 10 patients, in the Bellevue and University Hospital Surgical Service in New York. In all a prompt fall of arterial pressure and a gradual fall of central venous pressure occurred. In 8 patients there was an initial decrease in urinary flow and creatinine clearance with the fall in blood pressure, with a later return to control or higher levels. During this phase the sodium excretion was reduced. With a low blood volume, no improvement in renal function occurred until this had been corrected. In patients with cardiac abnormalities the main effect of the drug was a reduction in central venous pressure. Small intravenous doses cause a vasodilatation and extreme caution should be exercised in its use in vasoconstrictive states. Except in patients in a state of cardiac failure, a fluid infusion should always precede its use. Only small doses, 2·5 to 5·0 mgs., over a period of several hours, and never exceeding 10 mgs. should be given. A careful check of the blood pressure, central venous pressure and urinary flow should be done on every case.

Der Urologe

By JOHN GRIEVE

"**Post-traumatic Renal Artery Thrombosis.**" J. KAUFMAN and F. REINECKE. (1971, **10**, 273-275.)—In 2 cases of traumatic renal artery thrombosis there was no external evidence of vascular damage. There were few symptoms, little to be made out on urine examination, but poor or absent function on pyelography. Selective renal angiography is necessary for exact diagnosis and for possibly kidney-saving surgery.

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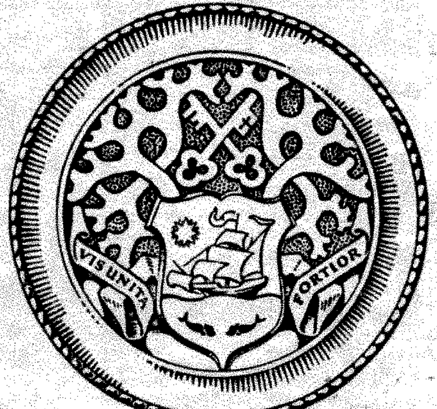

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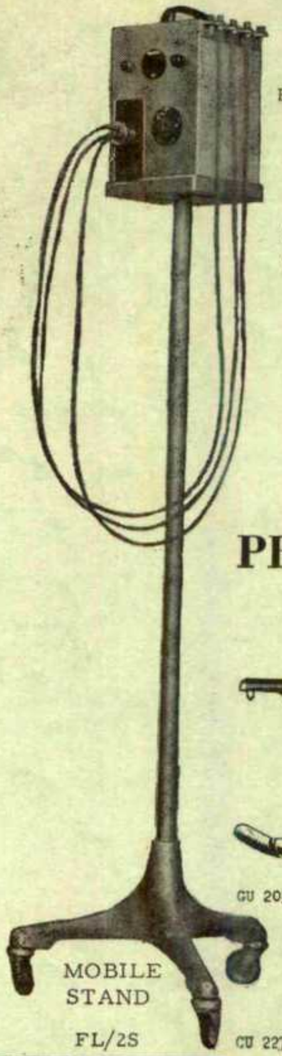

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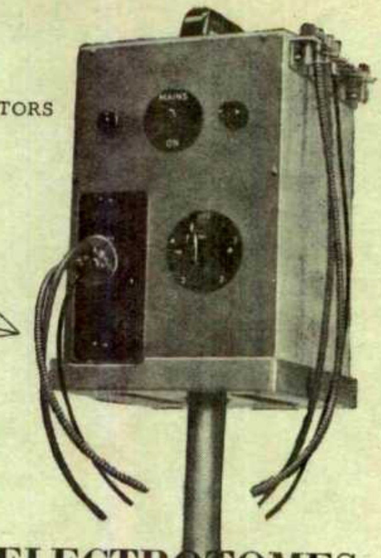

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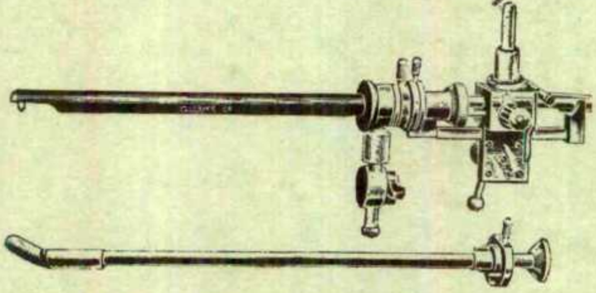

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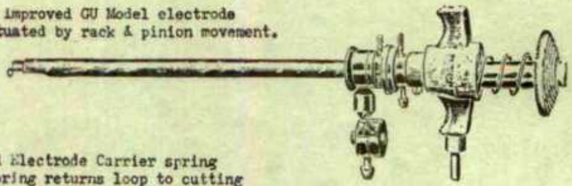

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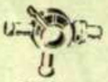

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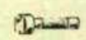

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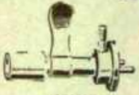

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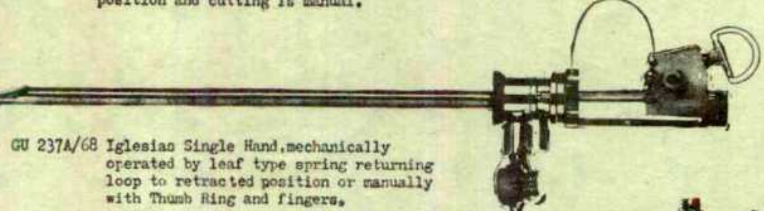

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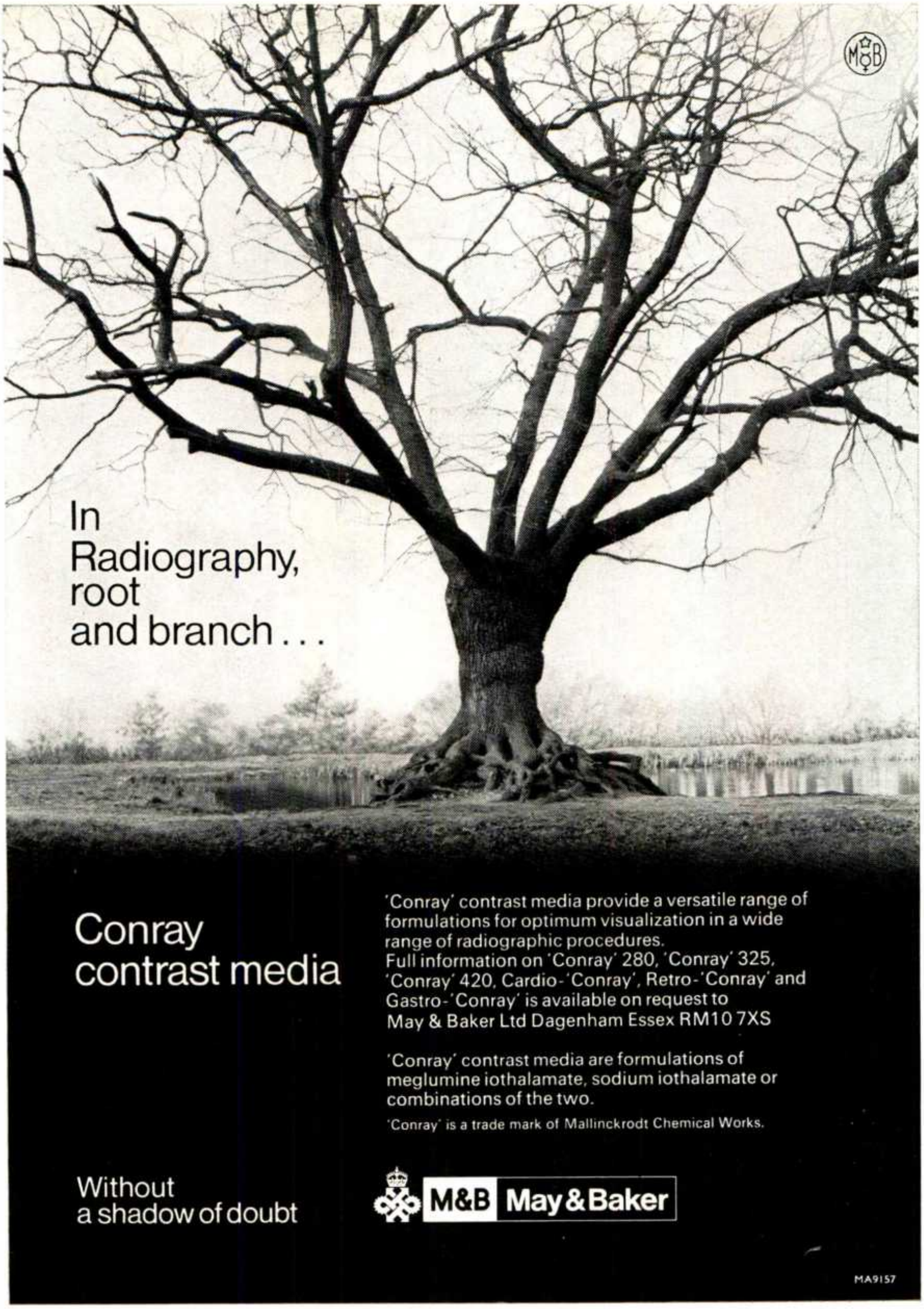

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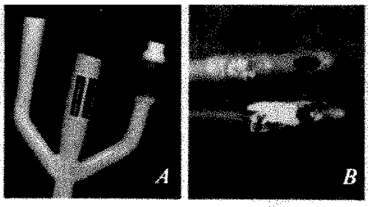

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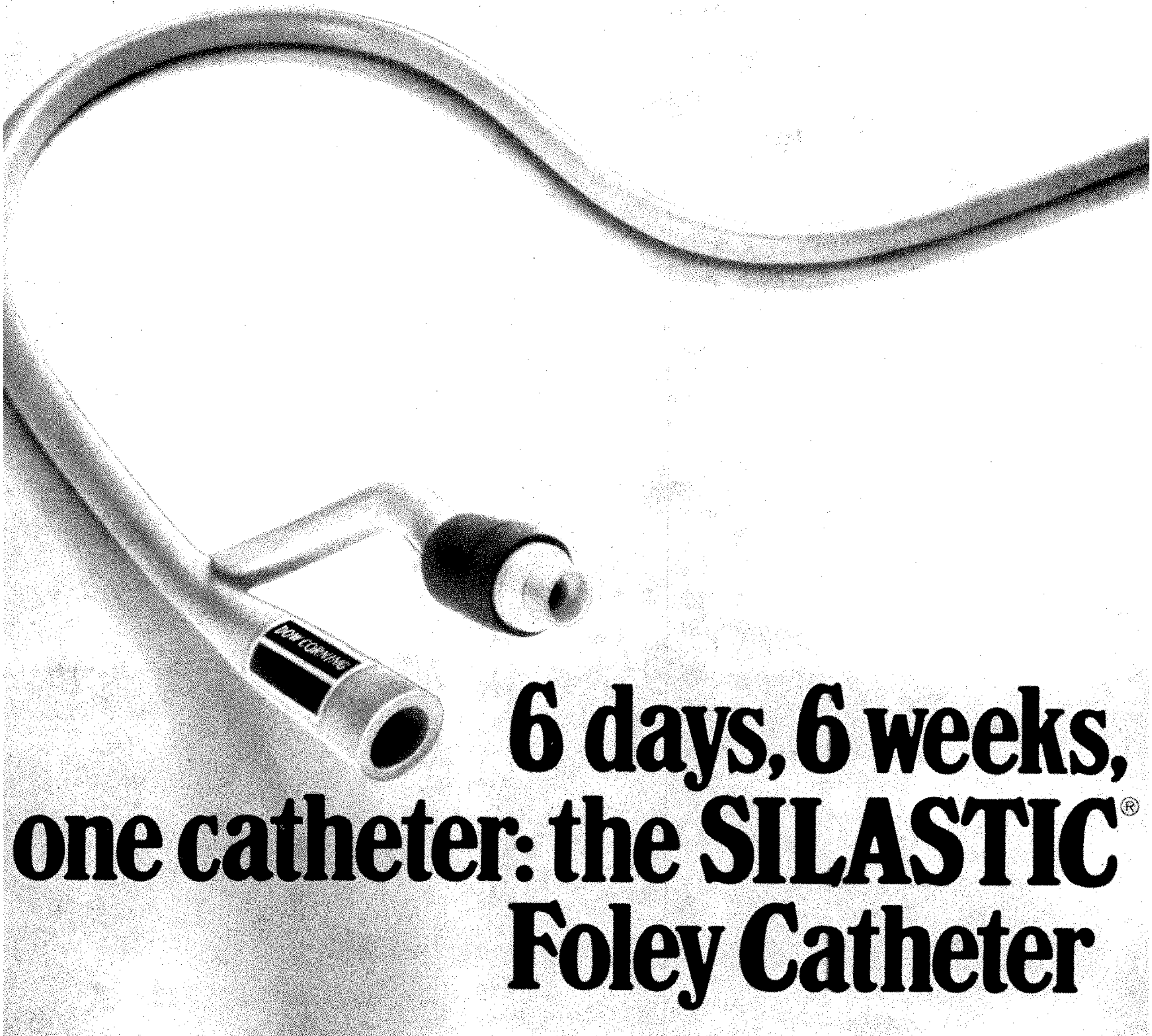

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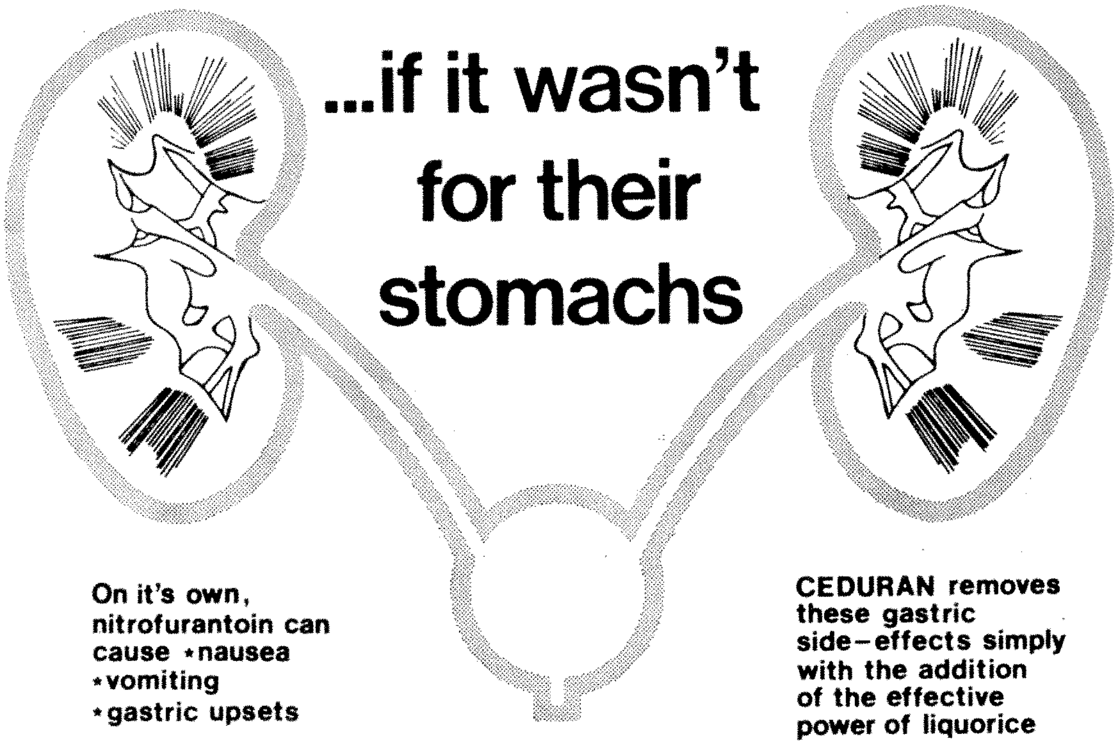

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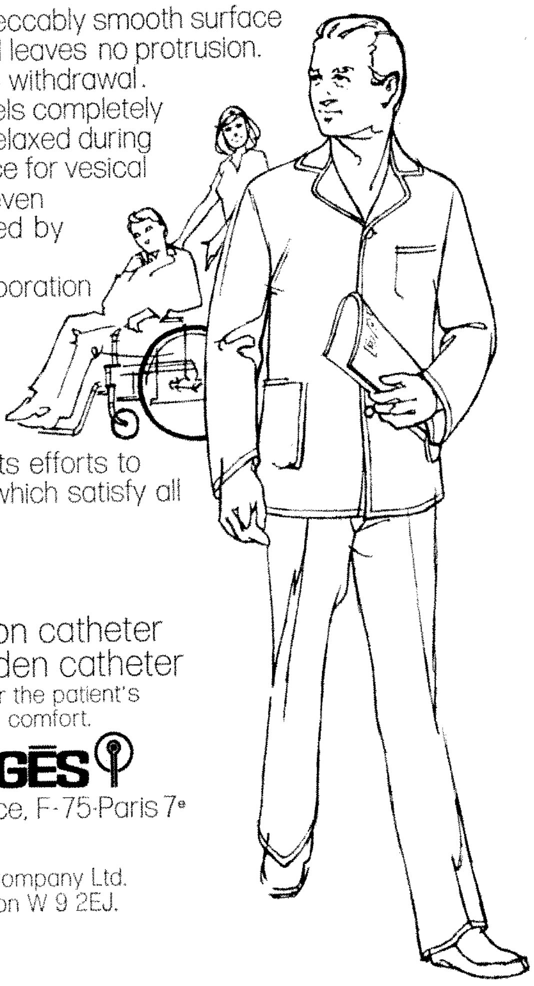

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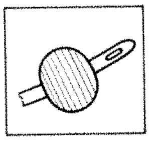

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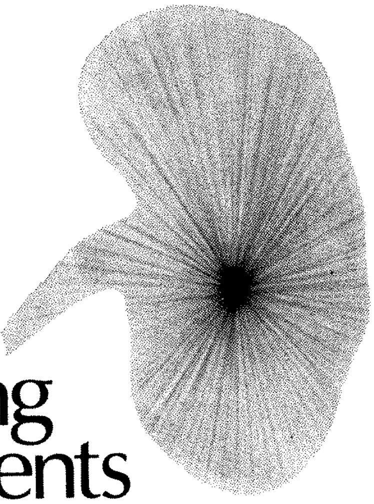

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1. *Clin Sci*, (1964), 27, 417.
2. *Clin Sci*, (1964), 27, 463.
3. *J Roy Coll Phycns Lond.* (1968), 2, 358.
4. *J Clin Endocrin Metab*, (1968), 28, 1829.
5. *Amer J Med*, (1971), 50, 67.
6. *Rev Clin Española*, (1970), 119, 61.

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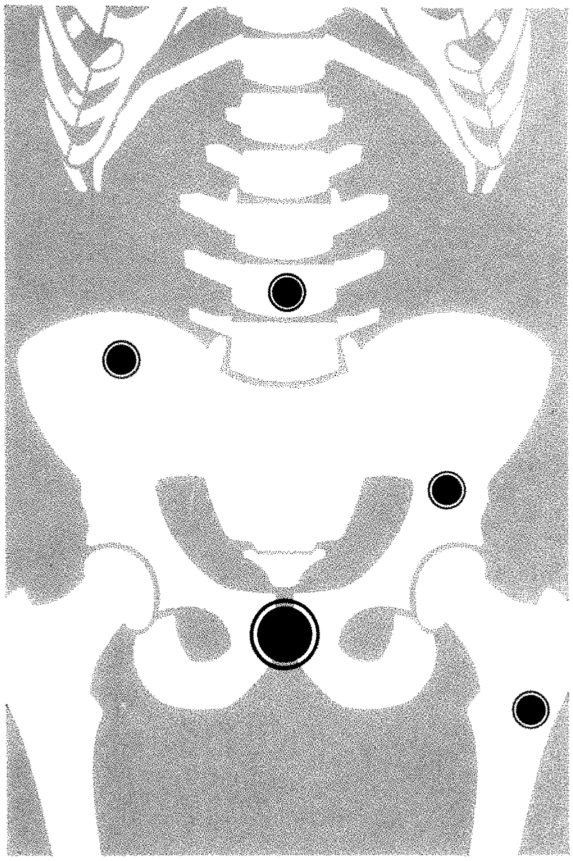

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1. *E.D.T.A. Proceedings*, VOL VI; (1969). 2. *British Journal of Urology*, (1970) **42**; 246. 3. *British Medical Journal*, (1969) **IV**; 717. 4. *British Journal of Urology*, (1970) **42**; 590. 5. *Lancet*, (1963) **ii**; 1143. 6. *J.clin.Path.*, (1964) **17**; 362. 7. Paper presented to the Dutch Ophthalmological Congress, Amsterdam, 1970. 8. *Lancet*,(1970) **ii**; 1116. 9. *J.clin.Path.*,(1964) **17**; 355. 10. *Arch.Dis.Childh.*, (1965) **40**; 235.

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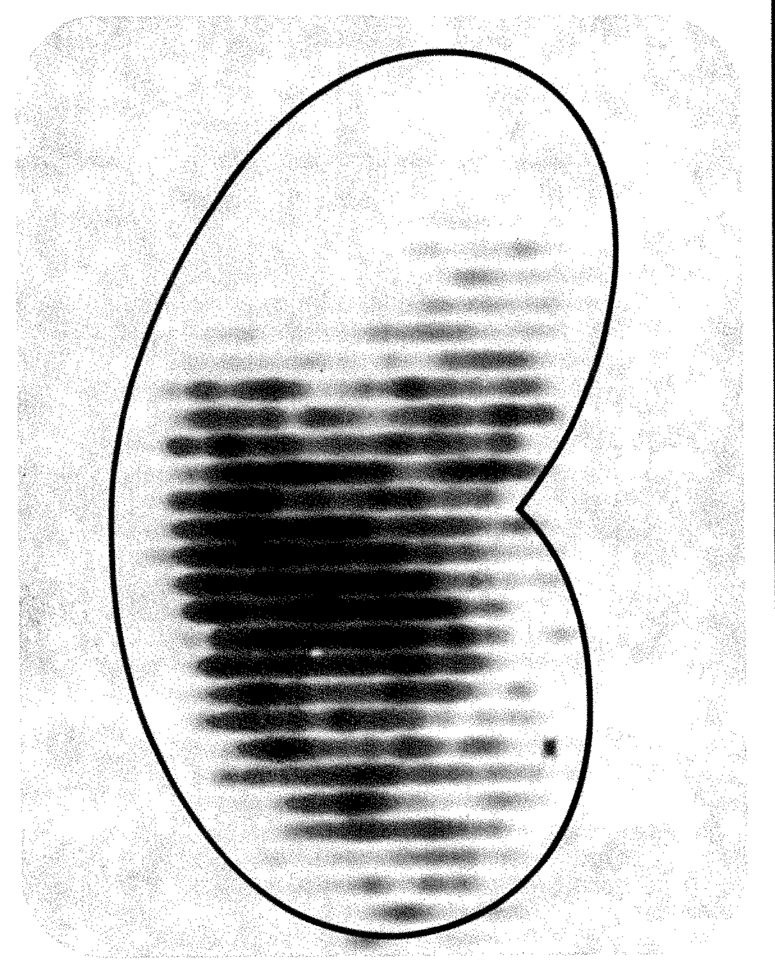

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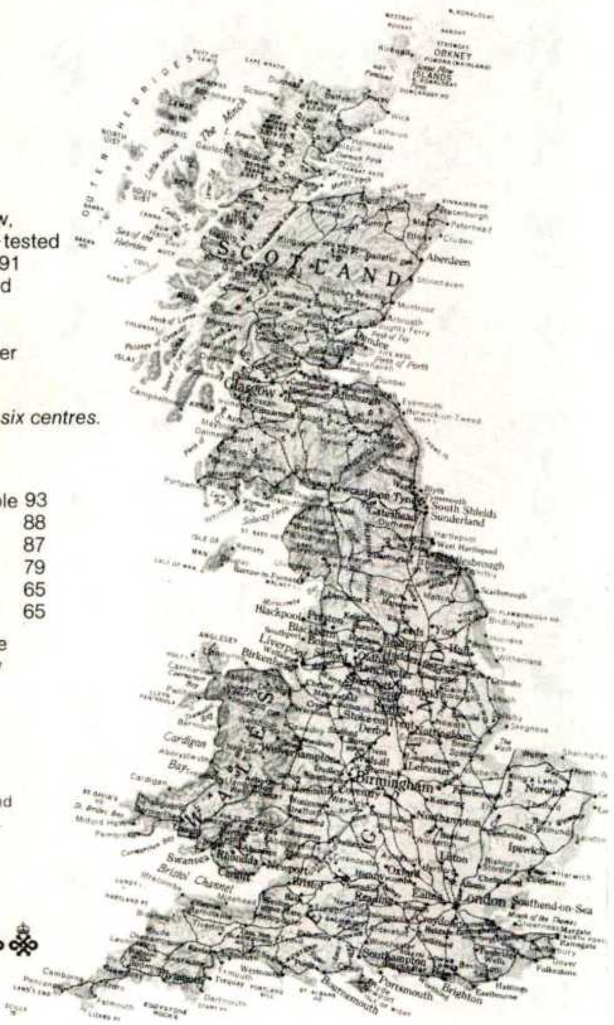

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(1) *Postgrad med J*, (1971), (September Supplement), *47*, 7.
(2) *Brit med J*, (1969) *i*, 541.
(3) Leading Article, *Brit med J*, (1969), *i*, 525.

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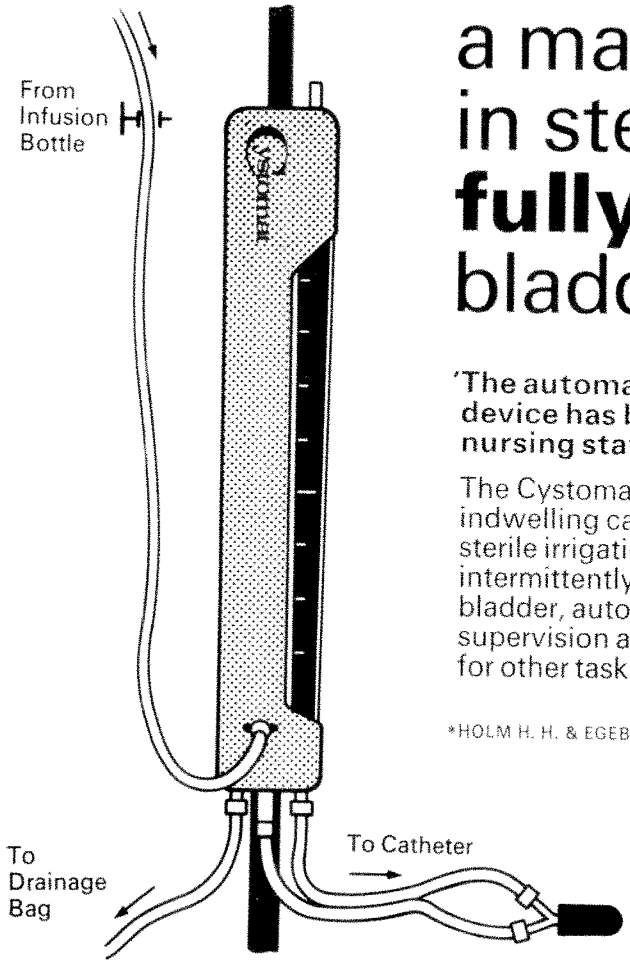

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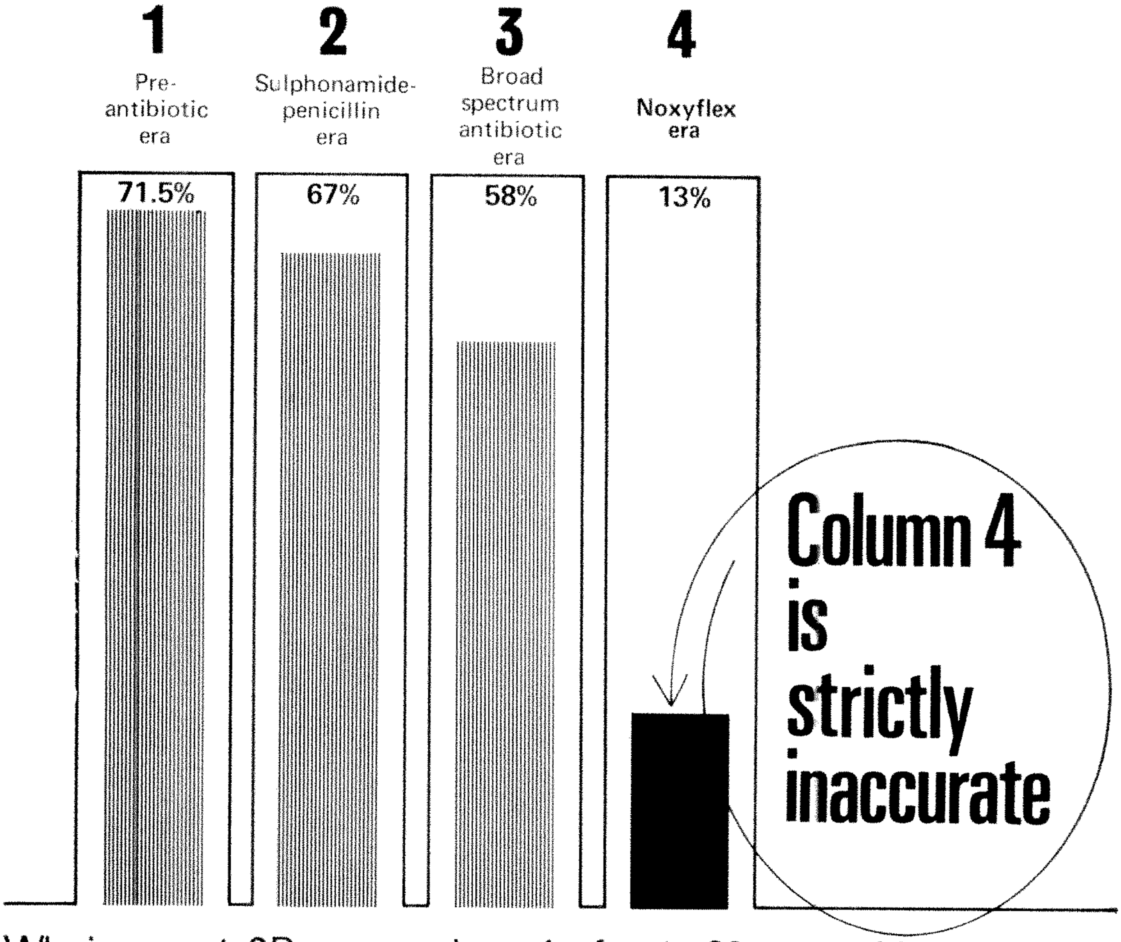

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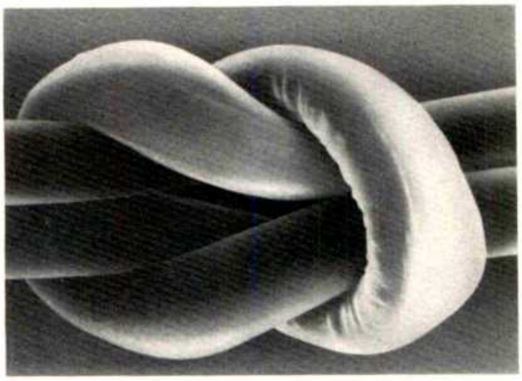

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1. Brit. Med. J., 1972, *3*, 13.
2. Brit. J. Clin. Pract, 1972, *26*, 341.

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Ultrasonic Laboratory, Department of Surgery H, Gentofte Hospital, Copenhagen, Denmark

THE first report on the application of diagnostic ultrasound to the kidneys was given in 1954 by Holmes *et al.* who demonstrated a kidney cyst with the aid of this new diagnostic principle.

Within the last five years there has been some mention of the use of ultrasound in the demonstration of renal masses (Holmes, 1966; Damascelli *et al.*, 1968; Goldberg *et al.*, 1968, Garrett *et al.*, 1970; Kratochwil *et al.*, 1970; Levi and Schulman, 1970; Schreck and Holmes 1970; Wehnert and Schentke, 1970; Goldberg and Pollack, 1971; Mountford *et al.*, 1971; Rand, 1971; Rosenberg *et al.*, 1971) but only recently a more systematic description of the ultrasonic picture of the normal kidney and its space-occupying lesions has been attempted (Barnett and Morley, 1971).

It is the aim of the present work to introduce a procedure for systematic examination of the kidneys with ultrasound. In addition, on the basis of five years' use of the method in our laboratory, to describe the ultrasonic characteristics of the normal kidney and the changes taking place with renal masses.

Principles of Diagnostic Ultrasound.—Sound at frequencies too high to be detected by the human ear is called ultrasound. Ultrasound at frequencies of about 2 million cycles per second can be transmitted through the human body as an almost cylindrical bundle of pressure waves. Ultrasound is generated in a transducer where a crystal is set into oscillations when exposed to electrical energy. This generation of ultrasound takes place several hundred times per second but each time only at the duration of about one microsecond. If the pressure waves created strike boundaries between various tissues at a right angle, part of the sound is reflected back in the same direction from where it came. Now the transducer serves as a receiver, converting the reflected mechanical sound waves into electrical energy which, after amplification, is displayed on an oscilloscope screen as vertical deflections from a horizontal base-line—so-called echoes. As the velocity of sound in human tissues is known, reflections from various depths in the direction of the sound beam can be displayed on the screen in a correct scale making it possible to measure distances within the body with great accuracy. This mode of ultrasonic visualisation is called A-presentation.

A two-dimensional impression of the interior of the body may be obtained if the transducer is moved in a previously selected plane of section and at the same time the position and direction of the transducer—and thereby the sound beam—controls the position of the electronic beam (the base-line) on the oscilloscope. When displaying the echoes in the form of bright dots on a fluorescent oscilloscope screen on which the dots remain for a certain length of time, an acoustical sectional image may be produced. This is usually known as ultrasonic scanning. By placing several sections parallel to each other or placing sections at right angles to each other a three-dimensional impression may be obtained.

Equipment and Technique of Examination.—For the A-presentation studies a modified Hewlett-Packard 7214A Diagnostic Sounder was used. For the recording of scanning pictures this apparatus was used in connection with an Escoline B-scanner and a modified Tectronix storage oscilloscope. The scanner consists of the transducer at the end of a triple-jointed rod system which, by means of potentiometers, ensures that the position of the electronic beam on the ocilloscope screen is in concordance with the position of the transducer.

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To facilitate the positioning of the scanner for the optimum sections, this can, automatically through a remote control, be displaced along a horizontal guide bar rail. Also the tilting can be varied through a remote control.

The complete set-up for ultrasonic scanning is seen in Figure 1.

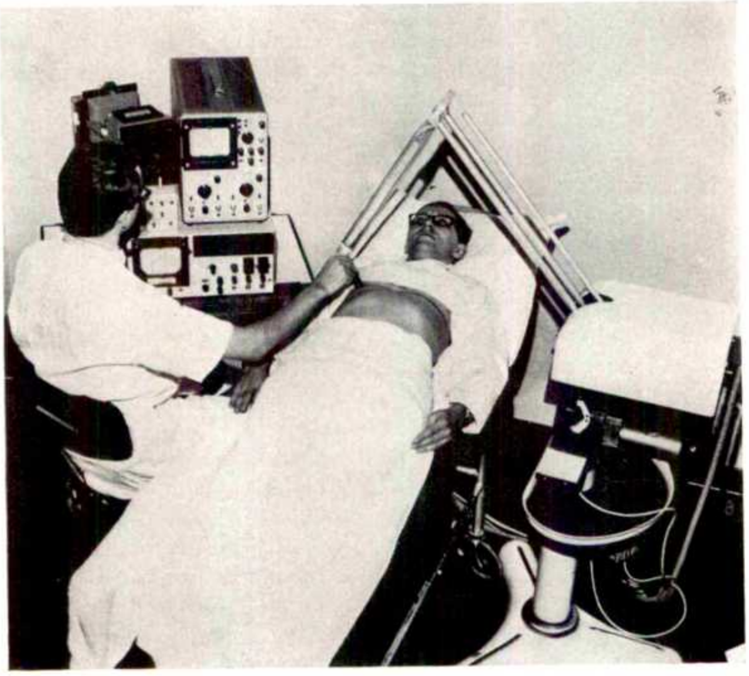

FIG. 1
Set-up for ultrasonic scanning.

In scanning pictures representing transverse sections of the patient in the supine position, the right side of the patient is displayed in the left side of the picture. In the prone position the right side of the picture corresponds to the right side of the patient. In longitudinal sections cephalad is always to the right (Fig. 2).

The patient may be examined in the laboratory on an examination couch or in his bed. If required the examination may be performed as a bedside procedure. The examination requires no preparation of the patient and it is without risk or discomfort.

To ensure good acoustic contact the skin is moistened with a thin film of oil and the transducer is then moved manually across the surface of the skin in the sectional plane chosen.

Routine examinations are performed with the patient in the prone position (Fig. 3). The upper and lower poles of each kidney are outlined and the centre projected vertically onto the skin where it is marked. In this way the longitudinal axis is defined and serial sections can be placed parallel to this axis. The tilting of the sectional plane has to be varied until the best representation of the kidney is obtained. On the longitudinal scans the inclination of the kidney in relation to the horizontal plane is found and so the tilting can be set for true transverse sections. Both longitudinal and transverse scans are carried out at intervals of 1 cm.

Some patients cannot be turned into the prone position, but still good transverse and longitudinal pictures of the right kidney are obtained with the patient in the supine position.

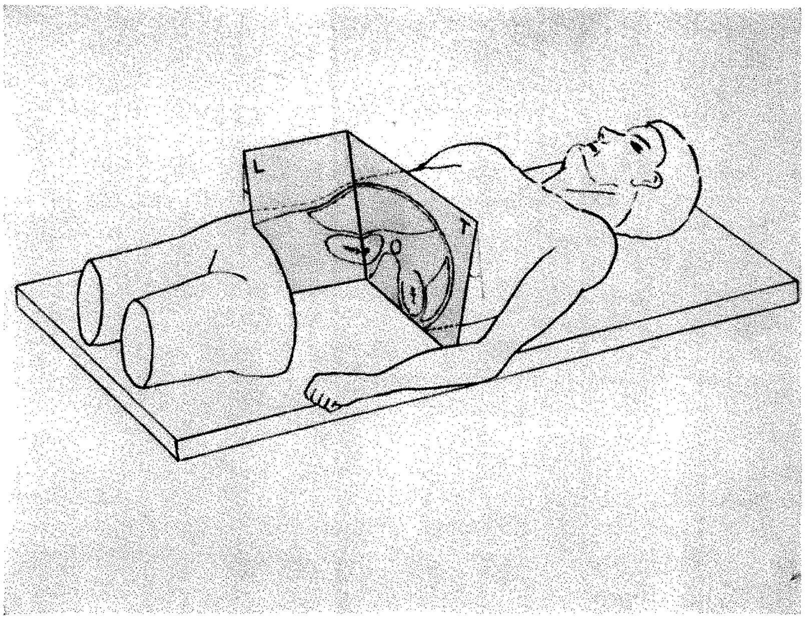

FIG. 2
Schematic illustration of the way in which ultrasonic sectional pictures are displayed. Transverse sections (T) as viewed from a caudad position, longitudinal sections (L) from the left.

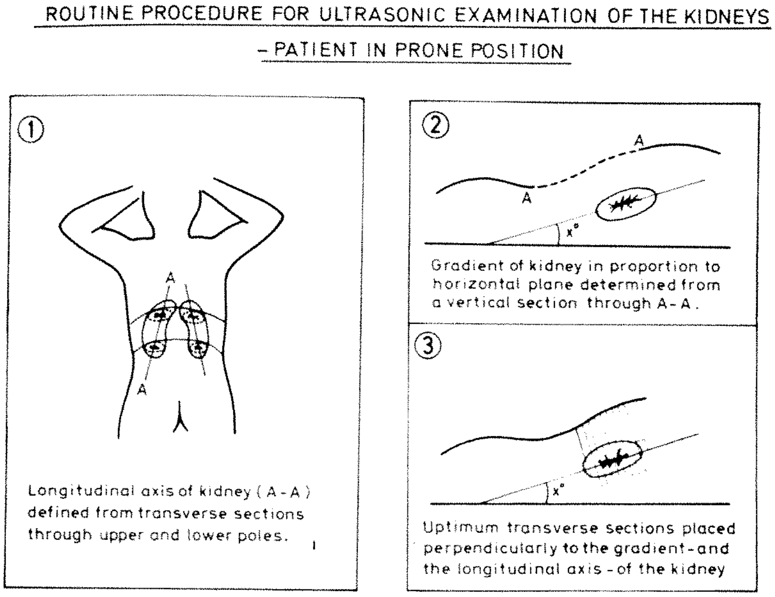
ROUTINE PROCEDURE FOR ULTRASONIC EXAMINATION OF THE KIDNEYS
- PATIENT IN PRONE POSITION
①
A
A
Longitudinal axis of kidney (A - A) defined from transverse sections through upper and lower poles.
②
A
A
x°
Gradient of kidney in proportion to horizontal plane determined from a vertical section through A - A.
③
x°
Uptimum transverse sections placed perpendicularly to the gradient - and the longitudinal axis - of the kidney

FIG. 3
Schematic illustration of routine procedure for ultrasonic examination of the kidneys: Patient in prone position.

This because the liver constitutes a good medium for the transmission of sound in contrast to the conditions on the left where, if gas filled, the stomach and bowel may hinder the penetration of sound. It may therefore be difficult to get a complete representation of the normal left kidney with the patient in the supine position, but when present, masses will often show up quite easily. In addition most patients can be turned on their side, making possible a scanning from the back.

Material.—The method for routine examination described above has been applied in our laboratory from October 1969. During the 2 years' period up to October 1971 approximately 500 kidneys were examined ultrasonically. The patients were referred from the various departments of the hospital and a few from other hospitals within the Copenhagen area.

A number of patients have been referred for ultrasonic examination as the initial investigation of the kidneys in cases of hæmaturia, lower back pain, a palpable mass in the flank or suspected occult carcinoma. A few have been examined because of hypersensitivity to radiopaque contrast media and some following radiographic procedures which had failed to give a sufficient detail of the kidneys or in which a proven mass could not be classified as solid or cystic. In addition the aim has been to examine ultrasonically all space occupying lesions of the kidneys demonstrated otherwise. Finally a few tumours and a number of cysts and hydronephroses have been diagnosed as accidental findings in patients who underwent ultrasonic scanning for other conditions.

A thorough evaluation of the reliability of ultrasonic diagnosis in renal masses is being undertaken on the basis of the above-mentioned material and will be published later.

The Normal Kidney.—The ultrasonic representation of various sections of the normal kidney is shown in Figure 4. The kidney is demarcated in relation to the surrounding tissues probably at the level of the fibrous capsule. For unknown reasons the fatty capsule of the kidney is usually not demonstrated ultrasonically, not even in obese patients. From an acoustic point of view the renal cortex is very homogenous and it only reflects sound to an extent registered by high levels of sensitivity of the equipment. In the centre of the kidney, dense echoes are registered, originating from the calyceal system, anteromedially confluent with equally dense echoes from the pelvic region. In normal conditions the pelvis is not sufficiently distended to show the echoes from its separated walls.

Renal Masses.—When examining the kidneys ultrasonically the following signs of space-occupying lesions should always be looked for:

1. break of the normal contour of the kidney,
2. dislocation of calyceal echoes,
3. areas which on increasing sensitivity of the equipment fill up with echoes, before the rest of the kidney,
4. areas which on increasing sensitivity of the equipment do not fill up with echoes,
5. splitting up of pelvic echoes,
6. splitting up of calyceal echoes.

Solid Tumours (Figs. 5, 6, 7).—Most tumours of the hypernephroid type are of a size that easily lends them to ultrasonic detection. Almost invariably they displace the calyceal echoes and break the contour of the kidney. Smaller ones may be poorly circumscribed and in any event solid tumours have a somewhat irregular demarcation. In addition, on increasing the sensitivity of the ultrasonic equipment, echo dots are registered inside a solid tumour before they are registered in the intact renal cortex. This acoustical lack of homogeneity of a solid tumour may often be better visualised on the A-presentation, on which numerous small echoes are seen corresponding to the area of the tumour.

Tumours arising in the renal pelvis may present with difficulty because of their frequent small size. When measuring 1 to 2 cm. or more they can, however, be demonstrated through

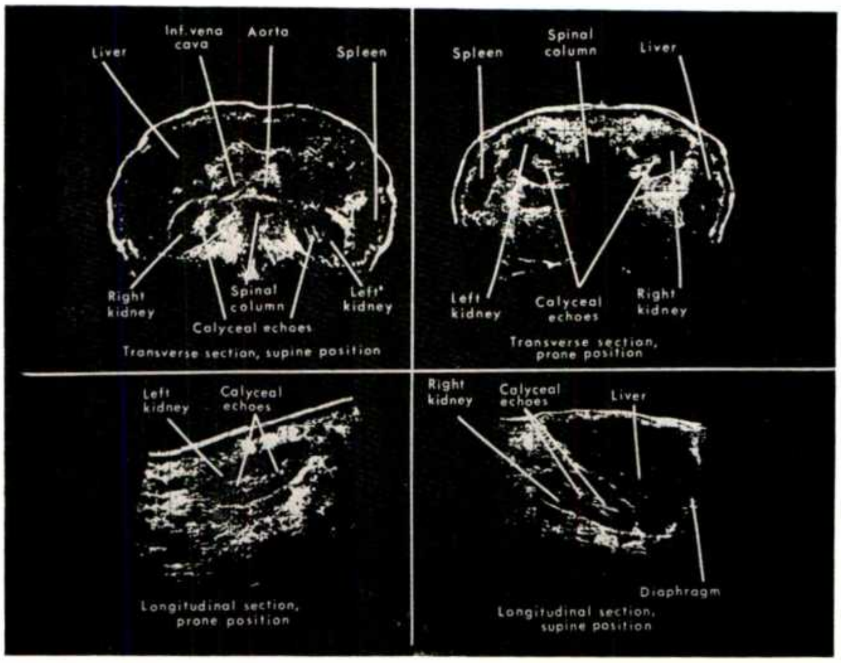

FIG. 4
Various sections of the kidneys in a normal subject.

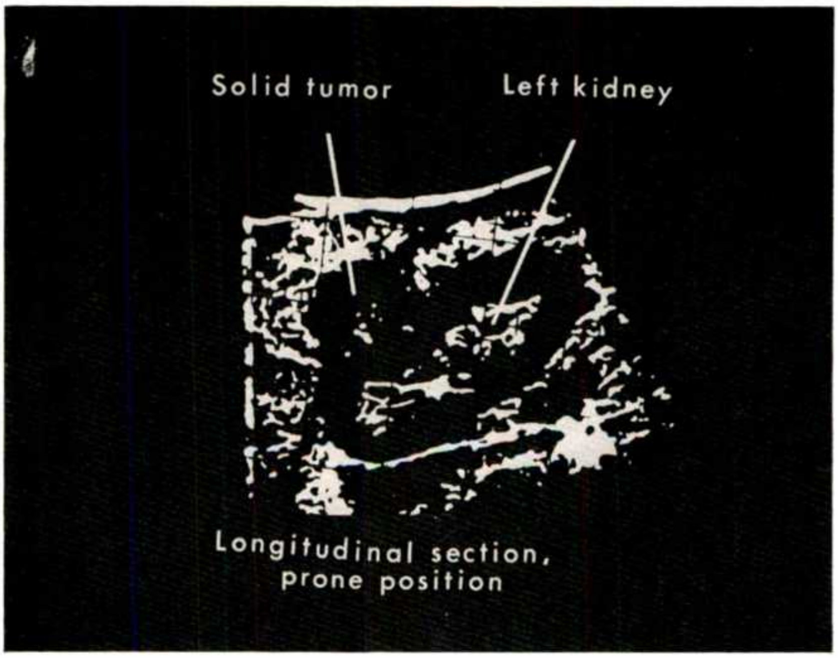

FIG. 5
Small process (4 cm. in diameter) protruding from the postero-lateral aspect of the kidney. Irregular demarcation and echoes inside the process denote a solid tumour.

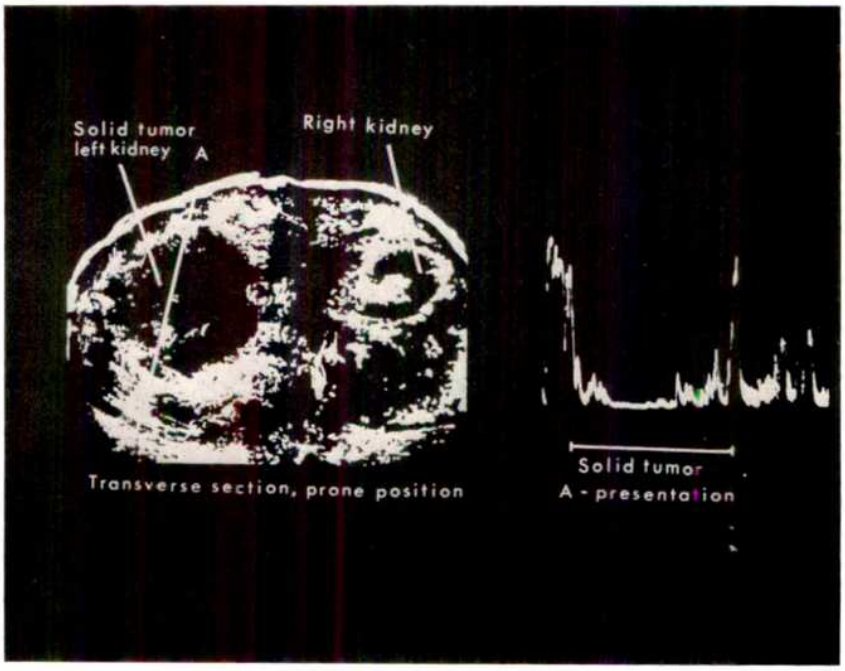

FIG. 6

Large process (10 cm. in diameter) extending from upper pole of the kidney. A-presentation in the direction indicated by the line A shows a solid pattern.

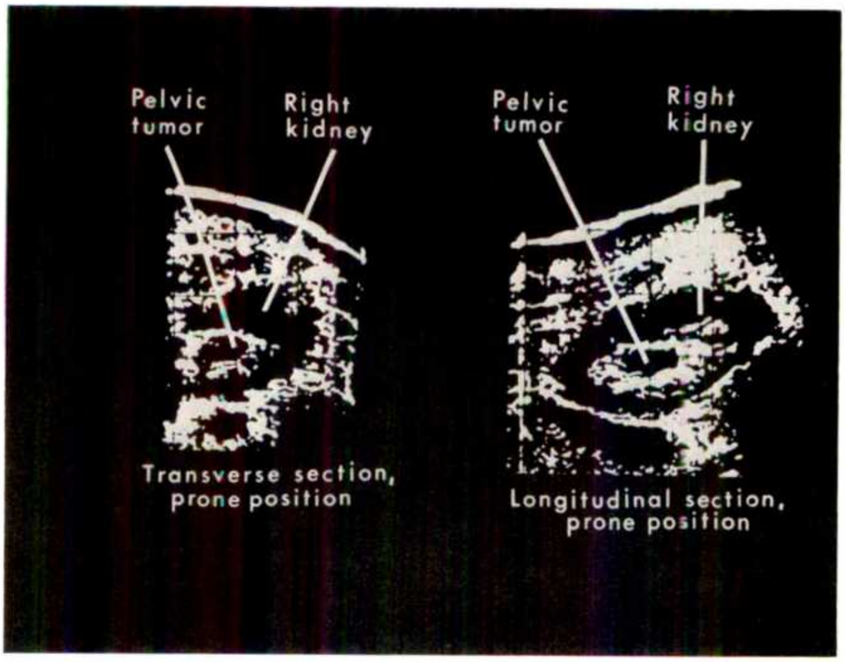

FIG. 7

Homogenous area (3 × 3 × 2 cm.) medially in the mid-portion of the kidney. The dense echoes from the calyceal system suggest a pelvic tumour rather than a hydronephrosis.

their splitting up of the pelvic echoes. Acoustically they are very homogenous and at their minimum detectable size it may be difficult to tell whether such a defect in the pelvic echoes represents a cystic or a solid area. If cystic this would indicate a dilatation of the renal pelvis and would almost invariably be accompanied by a splitting up of the calyceal echoes. An appreciation of this makes differentiation possible.

From a theoretical point of view ultrasonic differentiation between a pelvic tumour and a blood clot in the pelvis would not seem possible. No cases of clots have been encountered in this series. Pelvic stones are not visualised by themselves, but as they are impermeable to ultrasound, their presence may be suggested if there is an area within the pelvic region beyond which no echoes are visible—stones cast an ultrasonic " shadow ".

Solitary Cysts (Figs. 8 and 9).—Like solid tumours, solitary renal cysts most often appear in the ultrasonic picture as a break in the contour of the kidney in conjunction with displacement of the calyceal echoes. In large cysts the front wall is rather poorly defined whereas the back wall appears as a clearly demarcated curved line (Fig. 8). As there are no structures inside a cyst which reflect the sound the area of a cyst contrasts with the surrounding tissues in that the latter show up with numerous echo dots when the sensitivity of the ultrasonic equipment is increased.

It may be difficult in the ultrasonic picture to produce a clear-cut demarcation of smaller cysts (Fig. 9). These are best visualised by increasing the sensitivity of the equipment and looking for areas which do not fill up with echoes. When trying to outline such small areas it may be helpful to have the patient hold his breath while producing the picture because the movements of the kidney during respiration may completely obscure processes of the size of less than 2 or 3 cm.

In cases of doubt as to whether a process is cystic or solid the A-presentation may be more reliable than the scanning picture. Most equipments register that the amplitudes of the deflections on the A-presentation indicate the intensity of sound reflected to the transducer—intensity modulation—whereas in the scanning picture, only echoes of a certain strength are represented—the on-off principle. For a certain sensitivity setting of the ultrasonic equipment this means that weak reflections from the inside of a very uniformly composed tumour may not show up on the scanning picture but may very well be seen on the A-presentation. In order to evaluate properly such a picture the sensitivity level used in producing the picture should be known. No objectively measureable sensitivity levels have, however, been stated so far and so the evaluation has to rest upon a subjective impression of the sensitivity level. This is best obtained from the intensity modulated A-presentation.

Polycystic Kidneys (Fig. 10).—The ultrasonic picture of a polycystic kidney is that of a cystic area at the anticipated location in the kidney. The cystic area contains a number of rather distinct, straight or curved lines representing the mutual walls of the larger cysts. Collections of smaller cysts or areas of fibrous tissue may erroneously be taken for a solid tumour, and on the other hand it is difficult to detect ultrasonically a small, solid tumour in a polycystic kidney.

From the examination of one side of the patient only, a specific diagnosis cannot be made because a polycystic kidney and a large, mainly intra-renal hydronephrosis with caliectasia may both look the same in the ultrasonic representation. Supposedly a multicystic kidney presents with a similar picture, but such a condition has not been encountered in the present series. Bilateral findings almost invariably suggest polycystic kidneys, the development to such an extent of hydronephroses or multicystic kidneys on both sides being rather uncommon.

Hydronephroses (Fig. 11).—In normal cases the walls of the renal pelvis cannot be shown ultrasonically to be separated. In cases of slight urinary stasis (Fig. 11, A) a transverse scan will show a small homogenous area in the pelvic region. It may be difficult in such a picture to

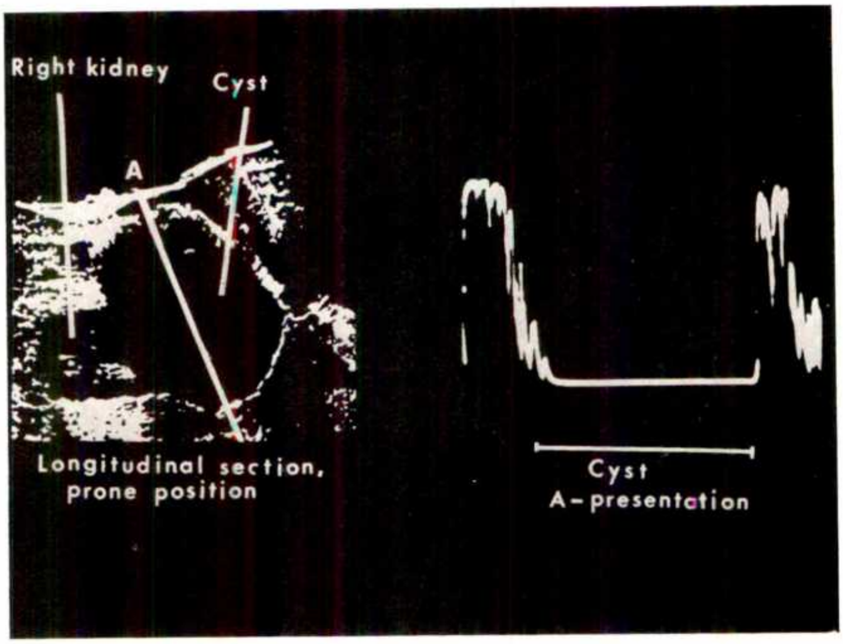

FIG. 8

Large process (10 cm. in diameter) in upper pole of the kidney. Back wall clearly demarcated and no echoes inside the process. A-presentation in the direction indicated by A shows a cystic pattern.

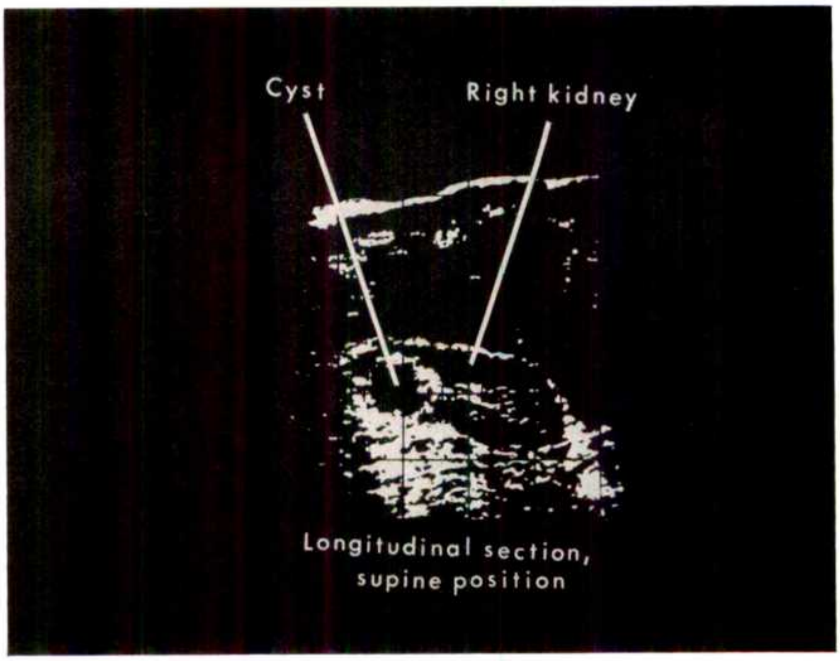

FIG. 9

Small process ($2\frac{1}{2}$ cm. in diameter) in lower pole of the kidney. Poorly demarcated walls but the process was not filled up with echoes when increasing the sensitivity of the ultrasonic equipment, denoting a cyst.

differentiate a solid pelvic tumour from a slight dilatation of the renal pelvis caused by urinary obstruction, but if on further ultrasonic examination, and this is best seen in longitudinal sections, a splitting up of calyceal echoes can be demonstrated, the latter condition is most likely.

More pronounced cases of hydronephrosis (Fig. 11, B) present with a very characteristic ultrasonic picture. On transverse scans a more or less circular and on longitudinal scans a more ovoid cystic process is seen. The calyceal echoes are split up and the kidney may be slightly enlarged but of normal shape.

In the ultrasonic picture a large extra-renal hydronephrosis (Fig. 11, C) appears as a large cystic process at the site of the kidney. In some cases a thin layer of homogenous tissue may be seen on its lateral aspect representing stretched renal tissue. This picture can be distinguished from that of an equally large cyst, because if the cyst is located in one of the poles of the kidney a normal opposite pole can be demonstrated. If a large cyst is located more centrally an area of dense echoes representing compressed renal tissue can, in most cases, be detected somewhere along the wall of the cyst, mainly medially.

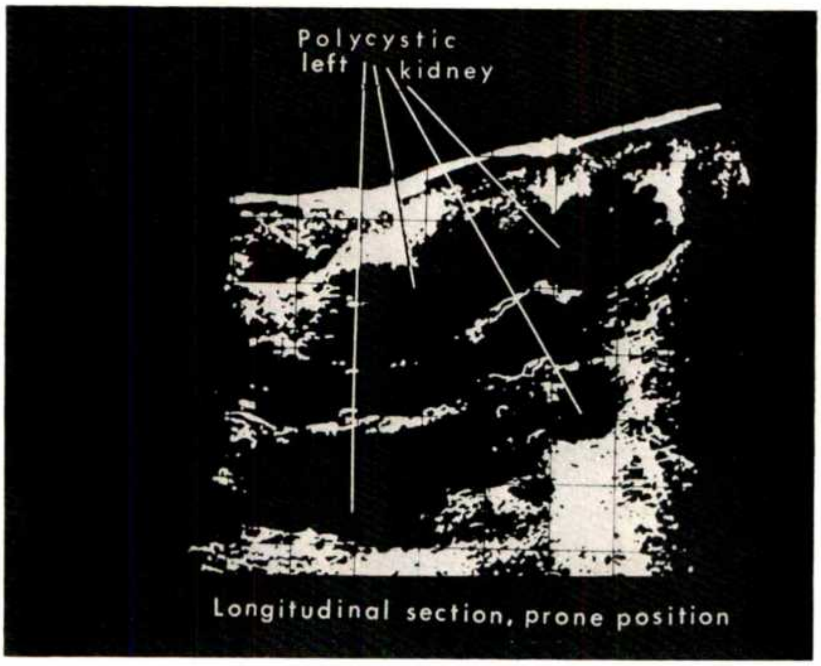

FIG. 10

Multiloculated cystic area at the anticipated location of the kidney. Similar picture on opposite side suggests a polycystic kidney. The condition cannot otherwise be differentiated from a large, mainly intra-renal hydronephrosis with caliectasia (Fig. 11, D) or a multicystic kidney.

If a hydronephrosis presents as a large multiloculated cystic process (Fig. 11, D) it cannot be distinguished ultrasonically from a polycystic or multicystic kidney (*vide supra*). Likewise it may be difficult in such cases to demonstrate or rule out minor tumour growth.

Conclusion and Summary.—Based on five years of experience with ultrasound in renal diagnosis—including 500 examinations within the last two years—a procedure is presented for routine examination of the kidneys for the investigation of possible space-occupying lesions. In addition a description is given of the ultrasonic picture of the normal kidney and the findings in renal masses.

It is possible ultrasonically to demonstrate hypernephromas, pelvic tumours, solitary cysts, polycystic lesions and all grades of hydronephrosis. Generally speaking, processes of the size of 1 or 2 cm. or more can be outlined on ultrasonic examination.

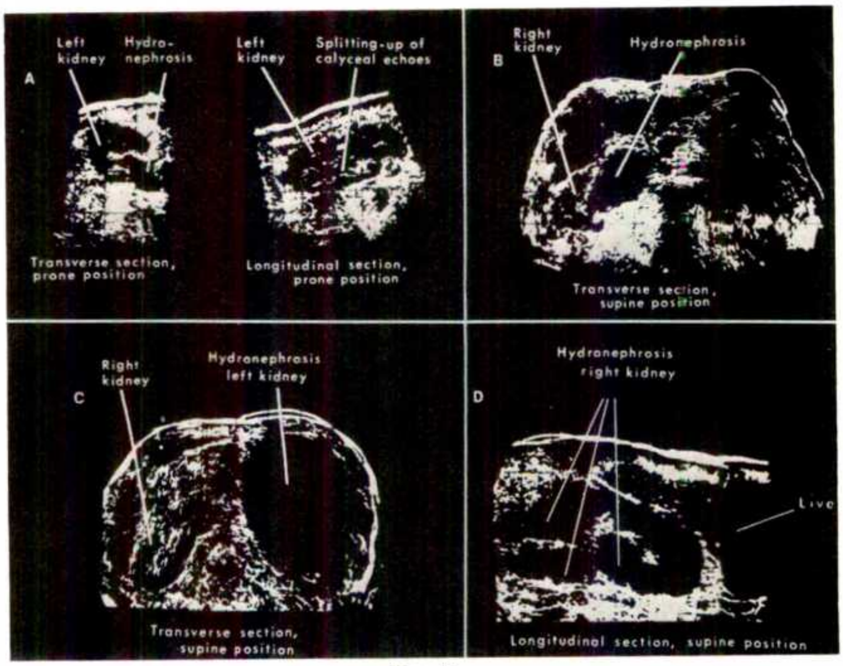
A
Left kidney
Hydro-nephrosis
Left kidney
Splitting-up of calyceal echoes
Transverse section, prone position
Longitudinal section, prone position
B
Right kidney
Hydronephrosis
Transverse section, supine position
C
Right kidney
Hydronephrosis left kidney
Transverse section, supine position
D
Hydronephrosis right kidney
Live
Longitudinal section, supine position

FIG. 11

A, Homogenous area in the pelvic region and splitting up of calyceal echoes demonstrate a small hydronephrosis. B, Cystic area extra- and intra-renally in the pelvic region, characteristic of a medium-sized hydronephrosis. C, Large cystic area at the level of the kidney which cannot be identified elsewhere denotes a large extra-renal hydronephrosis. D, Multiloculated cystic area at the anticipated location of the kidney. Normal kidney on opposite side suggests a large, mainly intra-renal hydronephrosis with caliectasia, but a multicystic kidney cannot be ruled out.

The accuracy of the method awaits further evaluation, but in our hospital this new diagnostic approach to renal masses has been found so valuable that it now forms an indispensable part of the investigations in surgical diseases of the kidneys.

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British Journal of Urology (1972), **44**, 528-531

IN SITU RENAL PERFUSION

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From The Royal Free Hospital, London

THE factors that influence the functional results of cadaveric renal homotransplantation are multiple, but we believe the most important is the duration of the initial warm ischæmic time. At the Royal Free Hospital, 44 renal transplants have been performed since October 1968. The average duration of the warm ischæmic period for these kidneys being 32 minutes. The subsequent duration of the cold ischæmic period seems to be less important: two of our patients have shown excellent function following transplantation 11½ and 18 hours respectively after donor nephrectomy.

Donor nephrectomy is performed by numerous teams in hospitals throughout this country. It is usually performed in an operating theatre but often one unfamiliar to the surgeon. The operation begins after cessation of cardiac activity. Time is known to be a factor of first importance, with the objective of removing the kidneys and cooling them as quickly as possible, and for this reason operative technique may be hurried. Where time is the master, the hazards of any surgical procedure are increased, and donor nephrectomy is no exception. Injury to the renal capsule, the renal substance, the ureter and its artery or the main vascular pedicle may result. The present technique of renal perfusion involves the insertion of a nozzle into the renal artery and this may result in damage to the intima, with subsequent spasm and delay in renal perfusion following revascularisation of the kidney.

***In situ* Renal Perfusion.**—As a result of experimental work in animals we believe that *in situ* renal perfusion can be easily and effectively performed with a substantial reduction in the warm ischæmic time and a subsequent unhurried anatomical donor nephrectomy.

Technique.—At the Royal Free Hospital we have devised an aortic double-balloon catheter. It has two inflatable balloons 5 cm. apart and 3 large eyes between the balloons as shown in Figure 1. Sizes 18, 24 and 28 F are available.

The catheter is attached to a perfusion apparatus before the onset of the operative procedure. The abdomen is opened through a midline incision from xiphi-sternum to pubis. The lower aorta is exposed and a right-angled vascular clamp applied across the aorta in its lower segment. The aorta is then opened proximally to the clamp through a vertical 1 cm. incision and the catheter introduced. The lower balloon is inflated below and as close to the renal arteries as possible and perfusion started. The upper balloon is then inflated about 5 to 10 seconds later, this period allowing most of the blood in the renal area to be displaced upwards in the aorta. Renal perfusion has now begun and the interval between cardiac arrest and renal perfusion should be approximately 5 minutes.

With this procedure the superior and possibly the inferior mesenteric arteries are also perfused. These vessels can now be ligated or clamped as near to their origins as possible. As renal perfusion progresses the pressure in the inferior vena cava gradually rises and better perfusion can be obtained if it is decompressed. A second double-balloon catheter is now introduced into the lower inferior vena cava using a similar technique and the balloons inflated above and below the renal veins. This catheter is connected to a drainage tube leading to a container on the floor (Fig. 2). As renal perfusion progresses it is possible to observe the efflux from the renal veins. Renal perfusion is continued for at least 10 minutes, when the colour of the kidneys can be observed and their temperature monitored if desired.

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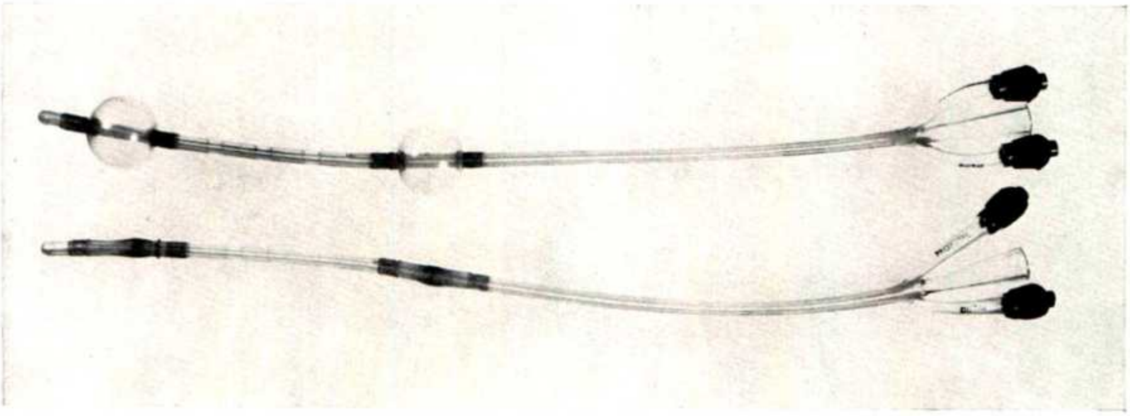

FIG. 1

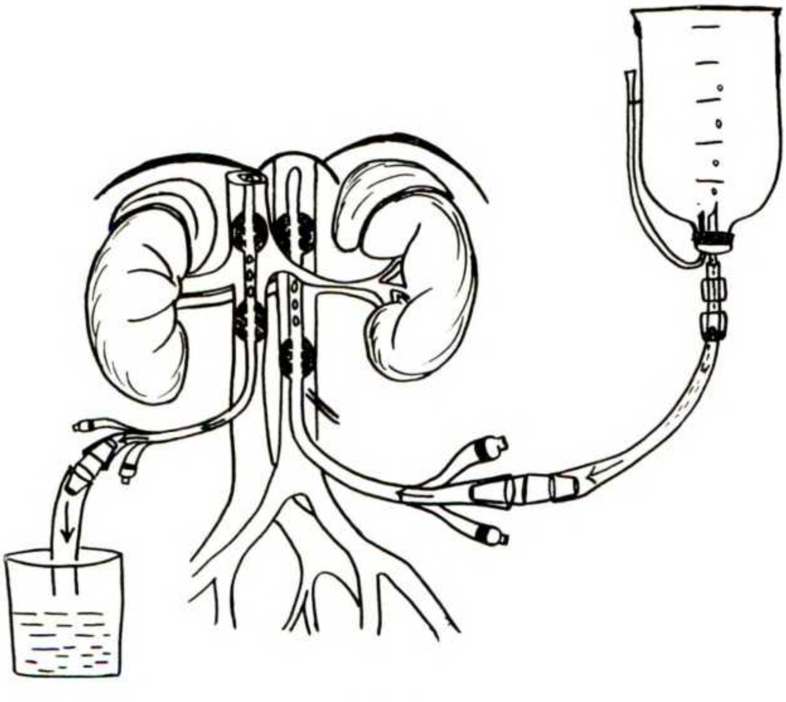

FIG. 2

Nephrectomy now begins. The renal capsule is cleared of perinephric fat. The ureters are displayed as far as the pelvic brim by reflecting the right and left colon, taking care not to dissect too close to the ureteric wall. The renal vessels can now be dissected up to the aorta and vena cava. The renal artery and vein can now be separated with a cuff of aorta and vena cava, and on division of the ureter the kidney can be removed. The aortic and caval catheters

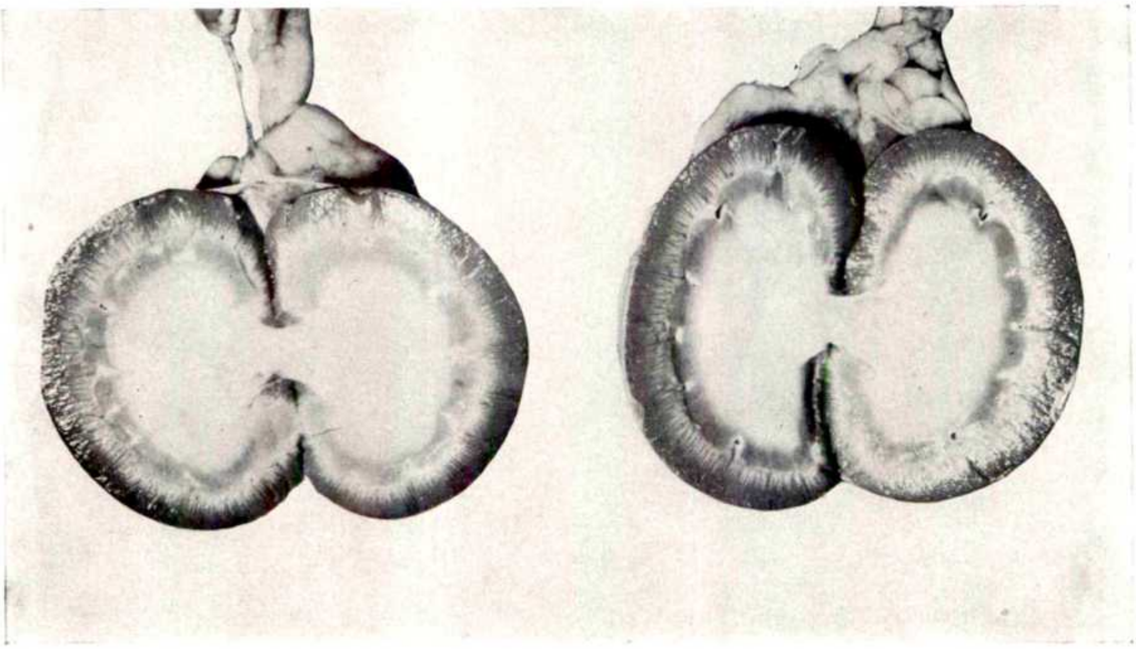

FIG. 3

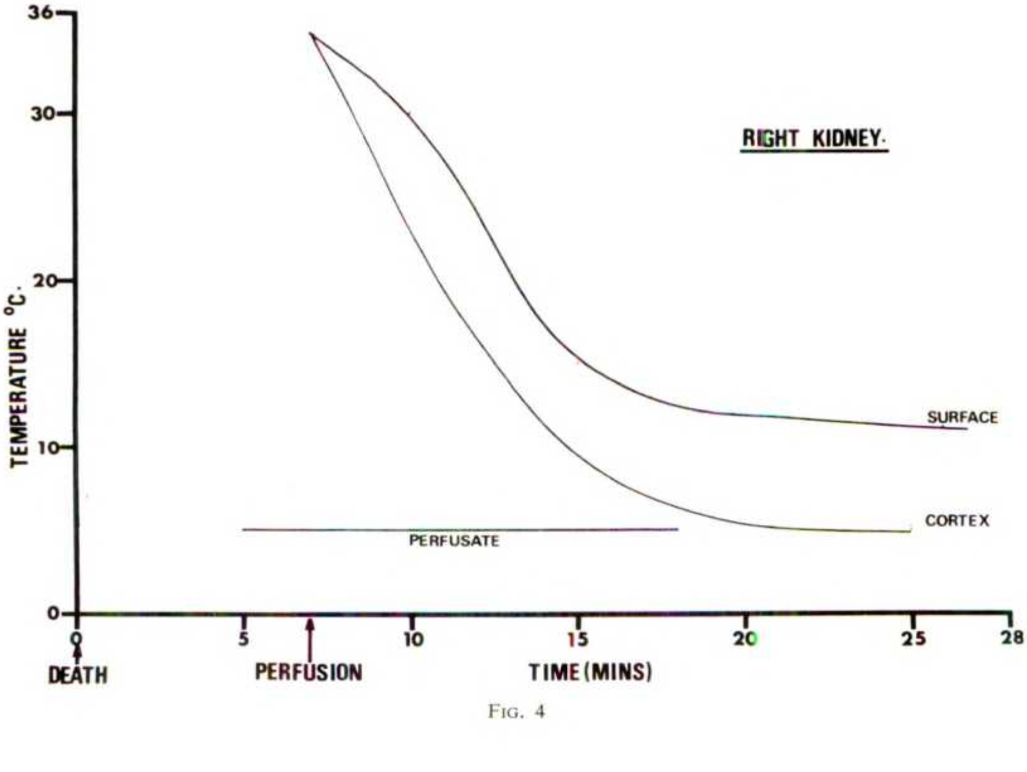
RIGHT KIDNEY.
TEMPERATURE °C.
36
30
20
10
0
SURFACE
CORTEX
PERFUSATE
0
5
10
15
20
25
28
DEATH
PERFUSION
TIME (MINS)

FIG. 4

remain and can be recovered after post-mortem examination is completed. The kidneys are now inserted into a sterile plastic bag and stored in ice for transport to the recipient.

Experimental Work.—This procedure has been performed on four mongrel dogs, using the technique described above. Renal perfusion was established in 7 minutes in each case. Figure 3 shows the kidneys removed after renal perfusion.

Temperature readings of the surface of this kidney, and the renal cortex, were monitored, using an electric thermocouple (Fig. 4). It can be seen that perfusion began 7 minutes after death and the renal temperature began to fall immediately. The cortical temperature dropped more rapidly than the surface temperature and reached that of the perfusate after 13 minutes. The surface temperature remained 3°C higher than the cortical temperature at all times. This pattern of renal cooling was found consistently throughout our experimental series. The duration of perfusion required to cool the kidney varied between 10 and 20 minutes.

We have had the opportunity to use this technique in one cadaver donor nephrectomy. The interval between circulatory arrest and completion of nephrectomy was 16 minutes and renal perfusion began 5 minutes after death. In both kidneys renal function began 2 and 4 days after transplantation respectively.

DISCUSSION

We believe that by using this technique of *in situ* renal perfusion with " The Royal Free Double-Balloon Catheter "[1] the duration of the initial warm ischæmic period can be reduced to less than 5 minutes. Donor nephrectomy can be carried out with less haste in the knowledge that the kidneys have been cooled already. Using this technique we feel that the anatomical and physiological state of kidneys removed from cadavers will be improved. This should result in earlier function of transplanted kidneys.

Our thanks are due to Mr R. Blackburn and Mr C. Marshall of Franklin & Sons Ltd and Miss S. Picton for Figure 2. We would also like to thank Mr C. Gilsen, Photographic Department of the Royal Free Hospital.

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[1] The Royal Free Double-Balloon Catheter is available from Messrs J. G. Franklin & Sons Ltd, Lane End Road, High Wycombe, Bucks.

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THE STRUCTURE AND FORMATION OF URINARY CALCULI: I. ORIENTED CRYSTAL GROWTH

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URINARY stones occur in a wide range of shapes, sizes, colours, composition and textures. They may be round, ellipsoidal, tetrahedral, highly irregular or shaped like a hempseed, mulberry or jackstone, etc. The surfaces may be rough, smooth, uneven or covered with large crystals. The smallest stones weigh just a few milligrams, the largest as much as a kilogram or more. Stones vary considerably in hardness: many crumble, others can be sectioned, while some cannot be ground at all. When a calculus is split open, the interior may show concentric laminated bands with or without radial striation, it may have a columnar pattern or it may consist of crystalline aggregates with no obvious structure. The many different substances which can crystallise from urine, their growth processes and their textures confer on stones their internal and external appearances.

The relationship between composition and the unusual shapes of some stones is well known (Prien and Frondel, 1947). Little attention has, however, been directed to a study of the growth of urinary calculi. As they are predominantly crystalline in nature (usually about 97 per cent of a stone is crystalline material), their formation is dependent on the laws of crystal growth. Modlin (1967) and Lonsdale (1968) postulated that epitaxy or the oriented growth of one crystal on another could be a factor in the growth of calculi. For epitaxy to occur, there must be a dimensional similarity between the faces of the substrate and deposit, and possibly some similarity of atomic arrangement in these faces. Calculations have shown that there are very close dimensional fits for some of the prominent crystal faces of the stone-forming substances (Lonsdale, 1968) and epitactic deposition is therefore possible on a suitable seed from a solution saturated with respect to one of these compounds.

As early as 1953, Carr examined microscopically the structure of 500 urinary calculi, unselected with regard to composition, and a special study by X-ray diffraction was undertaken of certain structural features, in particular the radial striation observed in approximately 25 per cent of the stones. Radial striation is frequently present in laminated stones consisting of calcium oxalate monohydrate, uric acid or brushite, and Carr made the interesting discovery that it was the result of the oriented growth of crystals along this direction. The crystals have a prominent crystallographic axis common to this direction but are randomly oriented about it. Preferred orientation was not reported for any other stone constituent.

In view of the possible importance of epitaxy and preferred orientation in stone growth, most of the other possible constituents have been examined to determine whether oriented growth is limited to the radially striated compounds studied by Carr.

Method.—Stones composed predominantly or totally of each of the stone-forming constituents were examined under a binocular microscope, and the different types of structure observed were also studied by X-ray diffraction. In the latter case, small pieces of material about 1 mm^3. or where appropriate, single crystals, were cut from the calculi and their positions in the stones noted. The hardness of many of the stones made removal of small samples and cutting of pieces already removed very difficult. The material was mounted on a glass fibre so that the axis normal to the stone surface was vertical. Since stones often tend to be ellipsoidal, this was not the radial direction except near the principal axes. The fibre was placed on a Unicam goniometer having a cylindrical camera radius of 3 cm., and the specimen was photographed using CuKα radiation. Exposure times were of the order of 1 hour. Photographs were taken with the specimen both stationary and rotating.

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If the material is a single crystal mounted and rotated about a prominent crystallographic axis, the resulting X-ray diffraction pattern shows small spots of varying intensity arranged on discrete " layer lines ". The separation of these parallel to the cylindrical film axis is related to, and thus gives, the identity distance along the rotation axis of the specimen which can usually be identified by this axial length, the nature of the substance being known. If the material is composed of many small crystals randomly oriented (a fine powder), diffraction occurs in a number of cones emerging from the specimen. The pattern as recorded on a cylindrical film then consists of rings each of nearly uniform intensity, but varying in intensity from ring to ring. The diameters and relative intensities of the innermost three or four rings can be used to identify the substances (Sutor and Scheidt, 1968). When, however, the crystallites are not randomly oriented, if, for example, they have some particular direction (which we call the fibre axis) parallel or nearly parallel, and this direction is the axis of rotation, the diffraction rings are broken into arcs whose spread is related to the amount of departure from parallelism of the crystals. Such crystals are said to show " preferred orientation " of the vertical axis but may have no preferred orientation about the axis. If the arcs have only a small spread, the picture is similar to that of a single crystal, and the layer line separation and thus the indices of the vertical fibre axis for crystals of known unit-cell dimensions can be determined by direct measurement. When the spread is large, individual arcs are, where possible, assigned the indices of the main planes giving rise to them, and from these and the positions of the arcs on the film, the indices of the fibre axis can be determined. In all our photographs both measurement of the layer-line spacing and the indexing of the diffraction pattern have been used to determine the preferred orientation axis.

Any orientation about the fibre axis can be checked either by remounting the specimen such that another direction is vertical, or more simply by taking a stationary photograph of the material in the original mounting. If the picture has the appearance of a rotation photograph of the substance, then the crystallites are randomly oriented about the fibre axis.

Results.—The oriented growth found in stones is given for each constituent. Unless otherwise stated, the fibre axis or direction of oriented crystal growth is perpendicular to the stone surface or preceding layer of material.

Uric Acid.—From X-ray photographs of four radially striated stones, the identity period along the fibre axis is 7·4 Å corresponding to the *b* axis, and the positions of the arcs on the photograph confirm this identification. (Uric acid is monoclinic, $a = 14{\cdot}46$, $b = 7{\cdot}40$, $c = 6{\cdot}21$ Å, $\beta = 65{\cdot}1°$.) The crystals are randomly oriented about this axis. Carr observed a fibre axis of the same length in the stones he studied, but was unable to identify it since the unit-cell dimensions of uric acid were not then known.

Uric Acid Dihydrate.—The hydrated form of uric acid is not as frequently encountered as the anhydrous one, and stones consisting mainly of this compound are uncommon. Pure or almost pure calculi are laminated and usually radially striated and in the two samples we studied, the axis of preferred orientation, approximately 17·6 Å long, is the *a* crystallographic axis. (Uric acid dihydrate is orthorhombic with $a = 17{\cdot}52$, $b = 7{\cdot}40$, $c = 6{\cdot}35$ Å.) As in uric acid there is no preferred orientation about this axis.

Calcium Oxalate Monohydrate or Whewellite.—The photographs obtained for the five laminated calculi studied have extended arcs, and the identity period of the axis perpendicular to the laminations could be measured only approximately as 17·6 Å. Whewellite is monoclinic with $a = 6{\cdot}28$, $b = 14{\cdot}57$, $c = 10{\cdot}11$ Å, $\beta = 109{\cdot}4°$. The positions of the arcs on the films show that the fibre axis is the 011 crystal axis which has a calculated length of 17·7 Å. Again there is no orientation about this axis. We have grown whewellite on glass fibres (Sutor, 1969; Sutor and Wooley, 1970; Dent and Sutor, 1971) and this had the 011 axis parallel to the fibre length. Carr found that the direction of radial striation in the five stones he studied had an identity period of $14{\cdot}1 \pm 0{\cdot}2$ Å, which he deduced was the *b* axis though the unit-cell dimensions of whewellite were unknown at the time.

Calcium Oxalate Dihydrate or Weddellite.—Usually this compound occurs in stones as single crystals of varying sizes and described as "envelope-shaped". These crystals almost invariably grow so that a sharp edge or sometimes a point is directed outwards from the centre of the calculus giving the surface a jagged appearance. X-ray photographs and the crystal morphology show that these directions are the *a* and 110 axes respectively. Weddellite is tetragonal, $a = 12{\cdot}30$, $c = 7{\cdot}34$ Å.

Magnesium Ammonium Phosphate Hexahydrate or Struvite.—This compound usually crystallises in stones as single crystals varying considerably in size. Under the microscope the small crystals form loose aggregates and the overall pattern is one of random orientation. This does not, however, preclude the possibility that a small crystal is oriented with respect to its neighbour. On the other hand, in a compact area of struvite which is usually a large single crystal and may even form a stone layer particularly on the surface, the *a* axis is perpendicular to the surface or previous band of material. Struvite is orthorhombic with $a = 6{\cdot}94$, $b = 6{\cdot}14$, $c = 11{\cdot}19$ Å.

In our collection is a group of about 100 small pure struvite stones from one patient, and they are composed of clusters of oriented single crystals from 2 to 5 mm. in length. The long axis of the crystals is the *a* crystallographic axis. Each stone started as one of these single crystals, then other crystals grew out perpendicular to *a* giving a star-like shape. In some cases, further deposition of material occurred between the crystals, and these stones are almost round except for the crystal ends projecting outwards.

Xanthine.—The five xanthine stones in our collection consist of very thin laminated bands of fine-grained material which is not radially striated. X-ray photographs indicate some preferred orientation in each stone, but this is not as pronounced as that shown by many other constituents since both the powder rings and the preferred orientation pattern are present on the photographs. The crystals are randomly oriented about the fibre axis which has an identity period of 3·55 Å but indices cannot be assigned to this direction since the unit-cell dimensions of xanthine are not known.

Ammonium Acid Urate.—Stones or areas of stones consisting entirely of this compound are rare. Generally the material is intimately mixed with other stone constituents usually the calcium oxalates or struvite. The few pure or almost pure stones in our collection, including a bladder calculus from a cat, are fine grained and laminated with radial striations. There is oriented crystal growth in all the calculi. In the cat stone consisting entirely of ammonium acid urate apart from a tiny nucleus of quartz and calcite (Jackson and Sutor, 1970), the identity period along the fibre axis is approximately 3·5 Å. The same repeat distance for the preferred orientation direction was found in two other stones including one containing intermixed whewellite. However, a different orientation for ammonium acid urate was observed in a stone composed of this urate and uric acid. Photographs of a specimen of mixed composition show that the fibre axis of uric acid is the usual one (the *b* axis) but the identity period for ammonium acid urate is 9-10 Å. The same repeat distance was observed when fibrous crystals of this compound were grown in silica gel. In both orientations, the crystals are randomly arranged about the fibre axis. The unit-cell dimensions of ammonium acid urate are unknown.

Apatite.—The apatites (carbonate and hydroxy) are the calcium phosphates most frequently found in urinary calculi. Although they form fine-grained laminated stones, strong preferred orientation has not been observed. In photographs of two stones, apatite apparently shows very slight preferred orientation of the usual direction, but the effect may have resulted from absorption of the diffracted beam by the non-uniform calcium-rich specimen.

Calcium Hydrogen Phosphate Dihydrate or Brushite.—Brushite crystallises in stones as long silky needles, with the long axis approximately perpendicular to the previous band of material, and shows prominent radial striation. From X-ray photographs of a single crystal taken from a stone, the needle-axis is 6·23 Å in length and the positions of the spots are in accordance with this being the *c* axis. (Brushite is monoclinic with $a = 5{\cdot}81$, $b = 15{\cdot}18$, $c = 6{\cdot}24$ Å, $\beta = 116{\cdot}4°$.) In the stone these crystals are not aligned with any other axis parallel. Photographs of pieces of material from two other brushite stones confirm this orientation. From a measurement of layer line spacings, Carr reported that the identity period along the direction of radial striation is 5·9 Å corresponding to the *a* axis. We feel that in this case the measurement of spacings alone may have led to some ambiguity, particularly as the *a* and *c* axes differ by only 0·43 Å and may not be distinguishable if a preferred orientation photograph alone was used.

Cystine.—Cystine stones looking like large crystals or crystalline aggregates and often composed of very large single crystals have the *a* axis perpendicular to the surface. Cystine is hexagonal with $a = 5{\cdot}42$, $c = 56{\cdot}27$ Å. We also have examples of multiple cystine stones from three patients, which consist of laminated bands of small cystine crystals. X-ray photographs show preferred orientation of the axis perpendicular to the laminations, and the position of the reflections and the identity period along the direction (56·3 Å) indicate that *c* is the fibre axis. There is random orientation about this axis.

One stone with a central area of cystine oriented so that the *a* axis is perpendicular to the surface, has an outer layer of struvite oriented, so that its *a* axis is also perpendicular to the surface and so parallel to the *a* axis of cystine.

Whitlockite, sodium acid urate and octacalcium phosphate which are also constituents of urinary calculi were not found in amounts large enough to study any preferred orientation.

CONCLUSION

Urinary stone constituents occur in a variety of textures ranging from almost colloidal particles to large single crystals extending several centimetres in one direction. Cystine, brushite, weddellite and struvite often crystallise as single crystals which can be removed and studied, while uric acid, uric acid dihydrate, ammonium acid urate, xanthine, apatite and whewellite occur frequently as fine-grained powders. A particular compound does not always have the same texture in the same stone. Whatever the texture though, oriented growth has been found for most stone-forming substances in many calculi, with the possible exception of the apatites. The oriented growth is such that a prominent crystallographic axis is approximately along the radial direction of the stone, more precisely perpendicular to the preceding band of material, but the crystals are randomly oriented about this direction. The axis is not unique for a compound. Two orientations have been observed for cystine and ammonium acid urate, and our orientation for whewellite differs from that found by Carr. As it was not possible to study all stones and every substance under all conditions, other orientations may also be possible. In cystine stones, the orientation is apparently related to the texture of the material. An area composed of a large single crystal has the *a* axis perpendicular to the surface, while laminated bands of small crystals have the *c* axis in this direction. Other factors such as the composition of the substrate on which growth occurs may also influence the orientation adopted.

Oriented growth of one substance on another is also present in stones. Only two examples were studied: firstly, uric acid and ammonium acid urate and secondly, struvite on cystine. Dimensions of the faces in contact could be calculated for the latter pair only and these fit closely (5·40 × 56·28 Å (cystine) and 6·13 × 56·0 Å (struvite)).

We conclude that oriented crystal growth is much more common in calculi than previously thought. Probably all our stones composed entirely of or having areas predominantly of cystine, uric acid dihydrate, brushite, ammonium acid urate and xanthine show this phenomenon as do most struvite stones, except those composed of loose aggregates of single crystals. All laminated and radially striated calculi composed of uric acid or whewellite probably have oriented crystal growth perpendicular to the laminations, and weddellite single crystals in stones are oriented with respect to this direction. Our work provides experimental evidence that oriented crystal growth and epitaxy are important factors in the growth of urinary calculi.

SUMMARY

Compounds present in urinary stones have a wide range of textures and each substance does not necessarily have the same texture even in the same stone. In calculi, oriented crystal growth has been found for most of the constituents including uric acid, uric acid dihydrate, whewellite, weddellite, xanthine, cystine, ammonium acid urate, struvite and brushite. In many stones which contain areas of these pure substances, crystal growth is such that a prominent crystallographic axis is perpendicular to the preceding band of material. The crystals though are randomly oriented about this axis. In stones consisting of layers of different composition, the oriented growth of one layer on another has also been observed. Oriented crystal growth could, therefore, be an important factor in the formation of urinary calculi.

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URINARY OSMOLARITY AND EXCRETION OF SODIUM, CALCIUM AND MAGNESIUM IN PATIENTS WITH RENAL CALCULI

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MANY factors have been thought to predispose to the development of renal calculi such as hypercalciuria (Hodgkinson and Pyrah, 1958), urinary excretion of pyrophosphate (Russell and Fleisch, 1968), sodium (Modlin, 1967), and magnesium (Oreopoulos *et al.*, 1968). From an inter-racial study of the incidence of renal stones, Modlin (1967) concluded that the urinary sodium/calcium ratio and the probability of developing a kidney stone are inversely related. On the other hand, Oreopoulos *et al.* (1968) felt that the most important factor in the genesis of stones was the magnesium/calcium ratio in urine. Studies by Isaacson (1968) revealed that it is the relative amount of calcium in urine, in relation to other solutes, that leads to the precipitation of calcium salts in the urinary tract rather than to changes in the concentration of any single ion.

Renal stones, mainly of the calcium phosphate type, are very common in Malaysia. Although the population of the country is made up of three major ethnic groups with different dietary habits, the incidence of renal stones is more or less evenly distributed among the population. Since no previous studies have been reported from this part of the world on the excretion of calcium, sodium, and magnesium in normal people as well as in stone cases, we decided to investigate the urinary excretion of these ions in our stone cases. It was also felt that such an investigation might reveal some biochemical abnormality in the excretion of these ions in the stone cases. This report is concerned with such a study.

Materials and Methods.—The series consisted of 50 male patients hospitalised for treatment of calculi in the renal tract, confirmed radiologically. All the patients were ambulatory and were on their regular diets. The controls included 26 healthy, ambulatory patients admitted to hospital for various non-urinary ailments such as inguinal hernia, hæmorrhoids, hydrocele, etc. None of the controls had any previous history of renal stones or diseases involving calcium metabolism.

Twenty-four-hour urines were collected under toluene and stored at room temperature while awaiting analysis. The volume and pH of the 24-hour aliquot, the osmolarity, and the calcium, sodium, and magnesium concentrations in the urines of each of the patients and each of the controls were determined. In addition to the urines, venous blood was obtained from both the stone cases and controls at the end of the urine collection and the serum calcium was also measured. The following procedures were adopted for the various chemical estimations: sodium was determined by flame photometry with an EEL flame photometer (Varley, 1967); calcium, by titration with EDTA using Hydroxynaphthol Blue as indicator (Catledge and Biggs, 1965); magnesium, by a colorimetric method with Calmagite (Chauhan and Ray Sarkar, 1969); and osmolarity, by observation of the depression of the freezing point, with a Fiske osmometer. The pH's of the urine were measured with a glass electrode and a Beckman pH meter (Model 72).

All measurements were done at room temperature and the results obtained were subjected to an analysis of variance by the student " t " test.

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Results.—As can be seen from the Table the serum calcium in the stone cases did not differ to any great extent from that of the controls, and it would thus appear that none of the stone cases was due to overactivity of the parathyroid glands.

TABLE

Biochemical Values in Controls and Stone Cases

	Controls (26)	Stone Cases (50)	t	P
Volume (ml./24 hours)	1198±183*	1312±138	3·09	<0 005 >0·001
Osmolarity (mOsm /24 hours)	638 ±108	408 ±122	8·157	<0·001
Sodium (g./24 hours)	2·48 ±0·42	2·26 ±1·10	1·000	N.S.
Calcium (g./24 hours)	0·15 ±0 03	0·19 ±0·05	3 73	<0 001
Magnesium (mg./24 hours)	79·85 ±4·20	78·8 ±4 80	1·003	N.S.
Sodium/calcium ratio	16·83 ±3·12	12·15 ±2·42	3·29	<0·005 >0·001
Magnesium/calcium ratio	0·551±0·12	0·447±0·12	0·14	N.S.
Calcium/osmolar ratio	0·24 ±0·05	0·51 ±0·23	5·774	<0·001
Serum calcium	10 30 ±0·40	10·12 ±0 21	1·99	N.S.

Numbers in parenthesis indicate numbers of subjects.
N S. = Not significant.
*Mean±1 Standard deviation.

Though the stone cases excreted a greater volume of urine with a decreased osmolarity compared to the normals, the amounts of sodium and magnesium excreted were not significantly different. On the other hand, there was a significant increase in the amounts of calcium excreted by the stone patients. When the sodium/calcium ratios were compared, it was seen that this was significantly higher in the controls. On the contrary, the calcium/osmolarity ratio was raised in the stone cases. The magnesium/calcium ratios were not significantly different in the two groups.

DISCUSSION

The mean serum calcium of the stone cases was 10·12 mg./100 ml. serum, and this was not significantly different from that of the controls. The urine pH of all the stone cases was less than 6·5. Although the 24-hour urinary volume in the stone cases was greater, this might have been due to a larger intake of fluids by this group following medical advice and no significance should be attached to it.

The calcium excretion in the stone cases was significantly greater than that of the controls, although none of them had true hypercalciuria (>300 mg./24 hours). One of the factors that predisposes to renal stone formation is a high urinary calcium (Hodgkinson and Pyrah, 1958), and it is unlikely that this was the responsible factor in our cases since the calcium excreted was well within the accepted limits of normal. Studies by Peacock *et al.* (1968) suggest that excessive renal excretion of calcium is a compensatory mechanism resulting from an increased absorption of calcium by the gut. The dietary patterns of the adult Malaysian population is one with a low intake of milk and dairy products and this may, in part, account for the relatively low urinary calcium levels both in the controls and the stone cases.

With regard to the urinary excretion of sodium, Modlin (1967) has claimed that there is a reciprocal relationship between the sodium/calcium ratio in urine and the liability to stone formation. On the other hand, Robertson and his colleagues (1967), and Papadimitriou *et al.* (1968) have disputed this hypothesis. They argue that the sodium/calcium ratio elevation in normal controls compared with the stone cases is mainly due to relatively increased excretion of calcium by the latter group. There was no significant difference in the urinary excretion of sodium between our controls and stone cases. Although the sodium/calcium ratio was significantly elevated in the controls, this might have been, to a large extent, due to the higher levels of calcium in the urine of the stone patients. Further, though the dietary habits of the different ethnic groups of our population show varying intakes of sodium, the stones were equally distributed among them. It therefore seems unlikely that the liability to stone formation is governed solely by the sodium/calcium ratio.

From their studies on stone-formers, Oreopoulos *et al.* (1968) came to the conclusion that one of the important factors in the genesis of stone formation is a reduction in the urinary magnesium/calcium ratio. Evans *et al.* (1967) and King *et al.* (1968) also demonstrated decreased magnesium excretion in their stone cases. On the other hand, Modlin (1967) found no significant difference in the daily excretion of magnesium between the stone-free Bantus and the stone-forming Whites and he felt that there was no apparent relationship between the daily levels of urinary magnesium and the tendency to renal stone formation. The magnesium levels excreted as well as the magnesium/calcium ratio in our stone cases were not significantly different from the controls. Probably magnesium excretion *per se* had no bearing on the process of stone formation in this series.

With regard to the osmolarity of urine, Isaacson (1968) has shown that the ionic strength of urine is very closely correlated with the osmolarity. Further, he has also demonstrated that it is the calcium/osmolarity ratio, rather than the excretion of any individual ion, that determines the tendency to stone formation (Isaacson, 1969). Chambers and Dormandy (1967) have also come to a similar conclusion from a study of patients with nephrolithiasis. In the present series, when the calcium excretion was compared with the osmolarity of the urine, it was noticed that the calcium/osmolarity ratio was significantly raised in the stone cases. Although it might be argued that this might have resulted from an increased urinary output of water by the stone cases, it seems very unlikely since the urinary volumes in this group were not statistically much higher than those of the controls. Since the solubility of salts such as calcium oxalate and calcium phosphate increase with increasing ionic strength, it is only to be expected that when the ionic strength (and thus the osmolarity) decreases, the calcium salts would tend to be precipitated with formation of calcium stones. It would thus appear that it is the relative amount of calcium in urine, in relation to other solutes, that leads to stone formation rather than to changes in the concentration of any single ion as postulated by Isaacson (1969).

SUMMARY

Urinary osmolarity and excretion of sodium, calcium, and magnesium were determined in 26 healthy controls and in 50 patients with renal calculi. It was seen that the calcium excretion and the calcium/osmolar ratio were significantly elevated in the stone cases. The results obtained are discussed in relation to findings from other centres.

There was no significant difference in sodium or magnesium excretion between patients and controls.

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THE MANAGEMENT OF URINARY CALCULOUS DISEASE IN PATIENTS WITH DUPLICATED URETERS

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The anatomical and physiological peculiarities often associated with ureteral duplication increase the probability of calculous formation. These peculiarities tend to make calculous disease more severe, foster its complications, and frequently introduce difficulties into its diagnosis and management. During the last 15 years, significant advances have been made in the anatomy, physiology, diagnosis, and treatment of urinary tract disease associated with ureteral duplication. Yet calculous disease in patients with duplicated ureters has been mentioned only briefly in the literature (Payne, 1959; Campbell, 1963). The following presentation, based on the author's experience in the management of 20 such patients during the last 10 years, emphasises problems of diagnosis and surgical treatment.

CONCOMITANTS OF URETERAL DUPLICATION THAT ENCOURAGE CALCULOUS DISEASE

Most urinary tract disease that is associated with ureteral duplication is diagnosed in childhood or in early adulthood; but urinary calculous disease as a concomitant of ureteral duplication has not been reported in the young. The development of urinary calculi must therefore depend on factors additional to duplication. Once calculous disease is initiated, for whatever reason, the likelihood that it will persist and recur is increased by the high incidence of reflux and obstruction associated with ureteral duplication. Reflux and obstruction cause ureteral dilation and atony; these induce stasis and chronic infection—an ideal milieu for the formation and growth of stones. In this environment, a calculous in a renal segment may rapidly grow to staghorn size. If obstruction and reflux are not corrected, spontaneous passage or surgical removal of the stone will probably be followed by recurrence. Since the lower renal segment ureter is especially prone to reflux, it may be expected to be the more frequent site of calculous disease (Fig. 1, A) (Amar, Hutch and Katz, 1968).

Where one of the duplicated ureters (usually that of the upper renal segment) has an ectopic orifice, obstruction is most likely to occur at the distal end of the ectopic ureter (Fig. 1, B). Ureteral dilation often results, and may contribute to calculous disease in the upper renal segment. Where infection supervenes, it increases the probability of calculous formation.

Primary ureteral calculi often form in a ureterocele, which frequently occurs at the lower end of the upper renal segment ureter (Fig. 1, C). The calculous increases the degree of obstruction and probability of infection in the involved ureter, enhancing the likelihood of calculi in the upper renal segment.

If vesico-ureteral reflux existed before removal of a renal segment, it is likely to persist in the ureteral stump, leading to dilation of the stump and chronic infection. Like a bladder diverticulum, the stump may be the site of calculous formation (Fig. 1, D). The presence of a calculous perpetuates urinary infection, encouraging further growth of the stone.

In a bifid (incompletely duplicated) ureter, the junction of the two renal pelves (or of the pelvis of one renal segment to the ureter of the other segment; or the junction of the two ureters) may be narrow. This site of relative obstruction may cause the affected ureter or renal pelvis to dilate, thus contributing to calculous formation (Fig. 2, A, B). The significance of this type of obstruction must be considered when rendering treatment for the stone (see Treatment).

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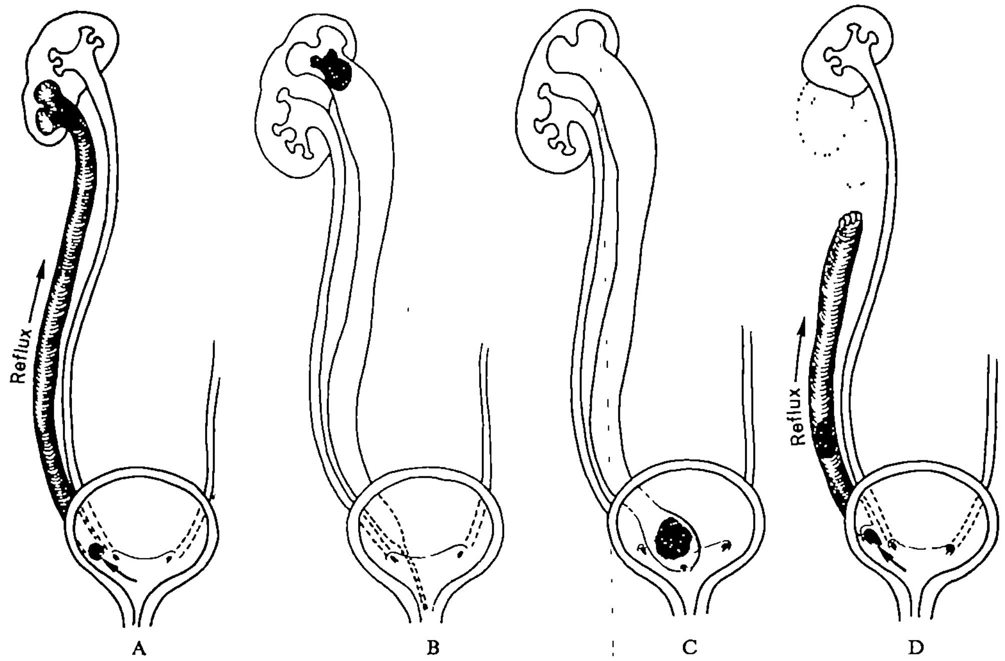


FIG. 1

Schema of the anatomical reasons for the increased likelihood of calculous disease in patients with complete ureteral duplication. A, Reflux into the lower segment ureter with renal atrophy and calculous formation. B, Ectopic ureteral orifice with obstruction at the distal end of the upper segment ureter, dilation of that ureter and its renal pelvis, with calculous in the involved renal segment. C, Ureterocele at the lower end of the upper segment ureter, containing a calculous. D, Calculous in the refluxing stump of lower segment ureter. The lower renal segment and attached superior portion of its ureter were removed because of chronic pyelonephritis.

DIAGNOSIS

Failure to suspect ureteral duplication when the patient is first seen with symptoms of calculous disease is illustrated in Figure 3. Where the upper pole renal pelvis does not visualise, the presence of a second ureter may be unsuspected. One may need to catheterise both ureters to establish the presence of duplication. If excretory urograms do not show both ureters satisfactorily, it may be difficult to discern which ureter contains the stone.

Calculous disease may be mistakenly diagnosed as tumour, renal cortical abscess, or other disease, leading to misdirection of treatment. For example, in the case illustrated in Figure 4, the upper renal segment failed to visualise on excretory urograms. The cause of failure proved to be a stone in the ureter of the affected renal segment. In the case depicted in Figure 5, the similar radiographic appearance proved to result from renal tumour. The presence of a perinephric abscess may obscure the diagnosis of stone in a duplicated ureteral system. Duplication may not be suspected until after extensive surgical intervention.

Where ureteral duplication is bilateral, calculous disease may be present in the upper renal segment ureter on one side, and in the lower renal segment ureter on the other. Or it may be in the common ureter below the junction of a bifid system. An example is shown in Figure 6.

Where the stone is in the common ureter below the junction of a bifid ureter, the calculous may induce different magnitudes of obstruction in the two limbs of the Y. In the renal segment

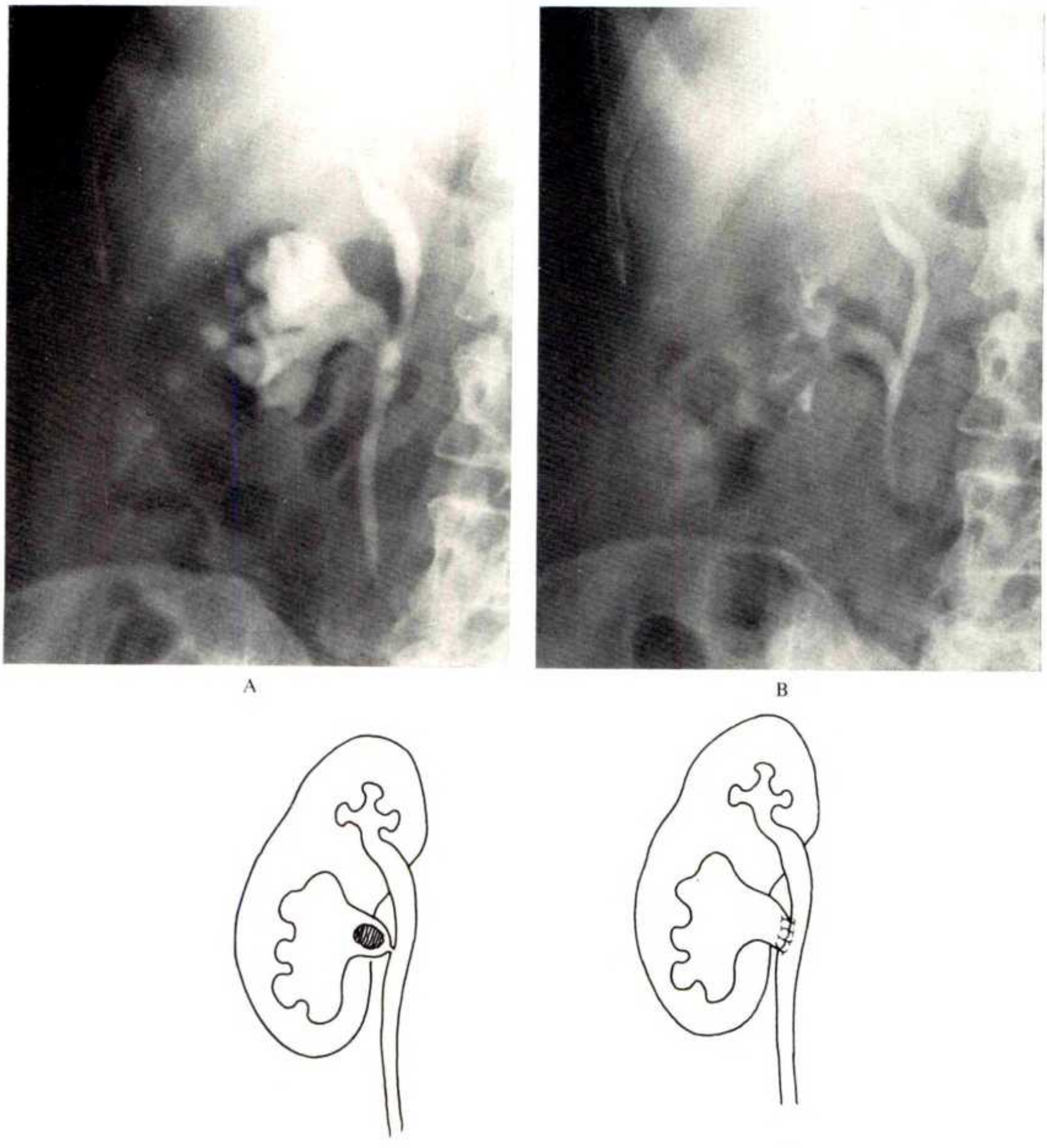


FIG. 2

47-year-old woman. A, Bifid right renal pelvis with stone in the lower renal segment. B, The junction of the lower segment pelvis to the upper segment ureter was narrow, necessitating pyelo-ureterostomy at the time of stone removal. C and D show the result of surgical treatment.

that is relatively protected from the effects of the obstruction caused by the calculous, the excretion of contrast medium may be better than in the other renal segment. To some degree it is possible to determine such a difference from the magnitude and direction of the uretero-ureteral reflux, and from the difference in functional reserve of the two renal segments. The upper renal segment is often smaller, and has less renal reserve, than the lower.

A stone may originate in one renal segment and migrate to the common ureter below the

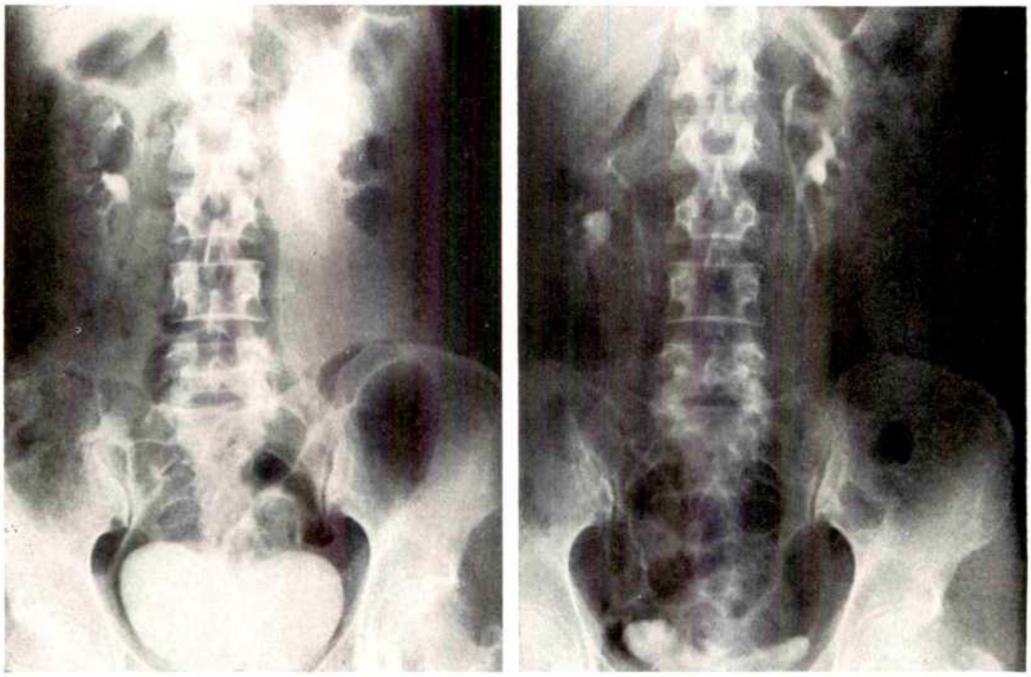


FIG. 3

35-year-old woman with left flank pain. A, Excretory urogram shows right ureteral duplication; extravasation of contrast medium into the peri-renal region on the left. Left upper pole calyx is seen; duplication unsuspected. B, Excretory urogram after spontaneous passage of the stone: bilateral ureteral duplication; normal renal function in all segments.

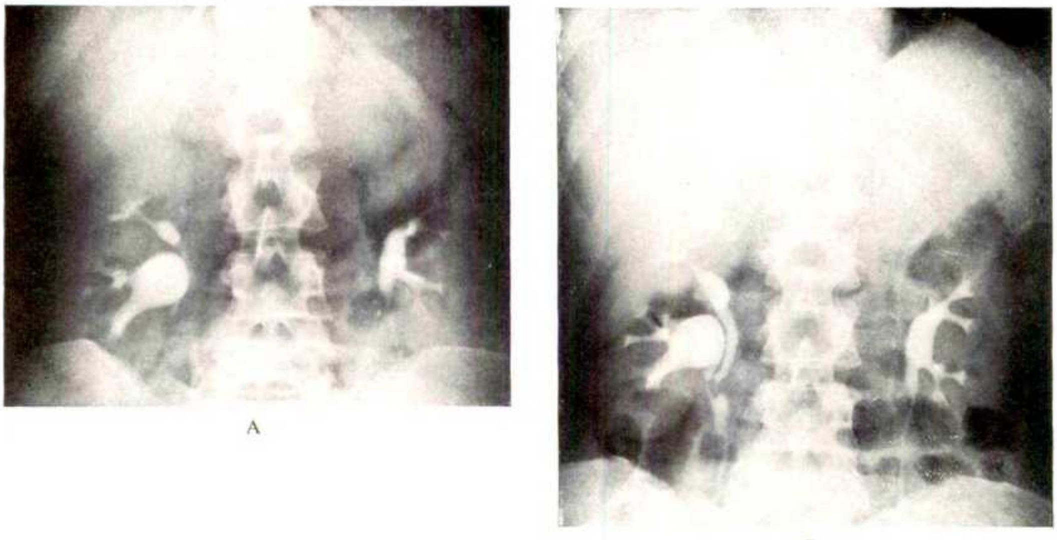
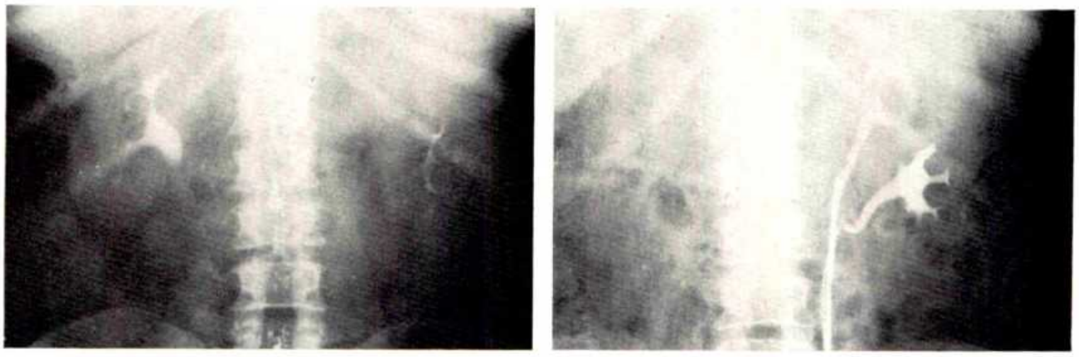


FIG. 4

35-year-old woman with left flank pain and microscopic hæmaturia. On the preliminary film of the abdomen (not shown) a calculous was faintly discernible against the sacrum on the left. A, Excretory urogram: right ureteral duplication; collecting structures visualise only in the lower part of the left kidney. Tumour in the upper part of the left kidney was suspected. The stone passed spontaneously. B, Excretory urogram now shows left ureteral duplication, explaining previous failure of visualisation of upper left renal collecting structures.



A FIG. 5 B

59-year-old man with left flank pain and hæmaturia. A, Excretory urogram shows normal right kidney. On the left, only the lower collecting structures are demonstrated suggesting calculous disease in the differential diagnosis. B, Retrograde uretero-pyelogram: tumour mass at upper segment of duplicated left kidney, which proved to be renal cell carcinoma.

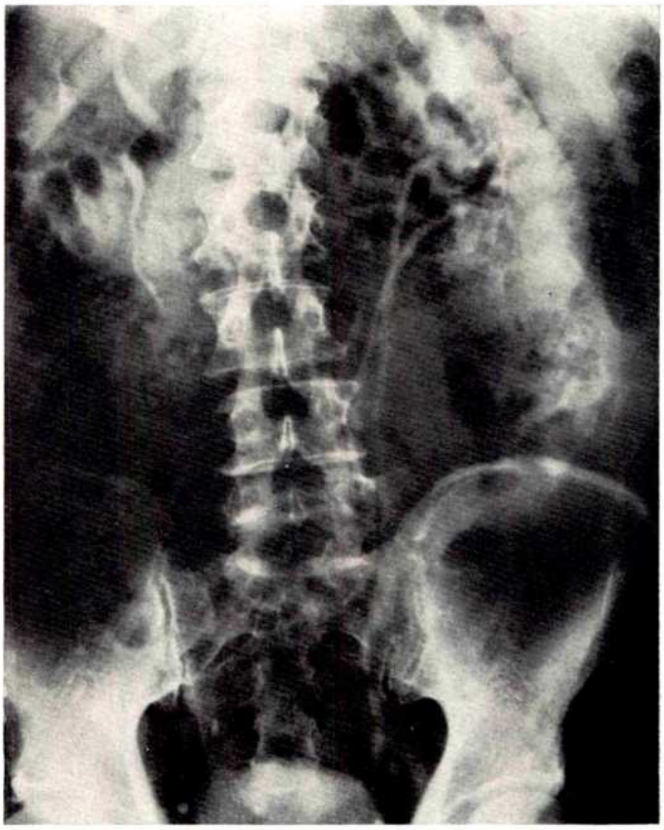


FIG. 6

Fig. 6.—32-year-old man with bilateral upper flank pain and microscopic hæmaturia. Excretory urogram shows bilateral duplication. A calculous obstructs the upper renal segment ureter on the right. Another calculous obstructs the common ureter below the junction of the bifid ureter on the left. Passage of both calculi confirmed the diagnosis.

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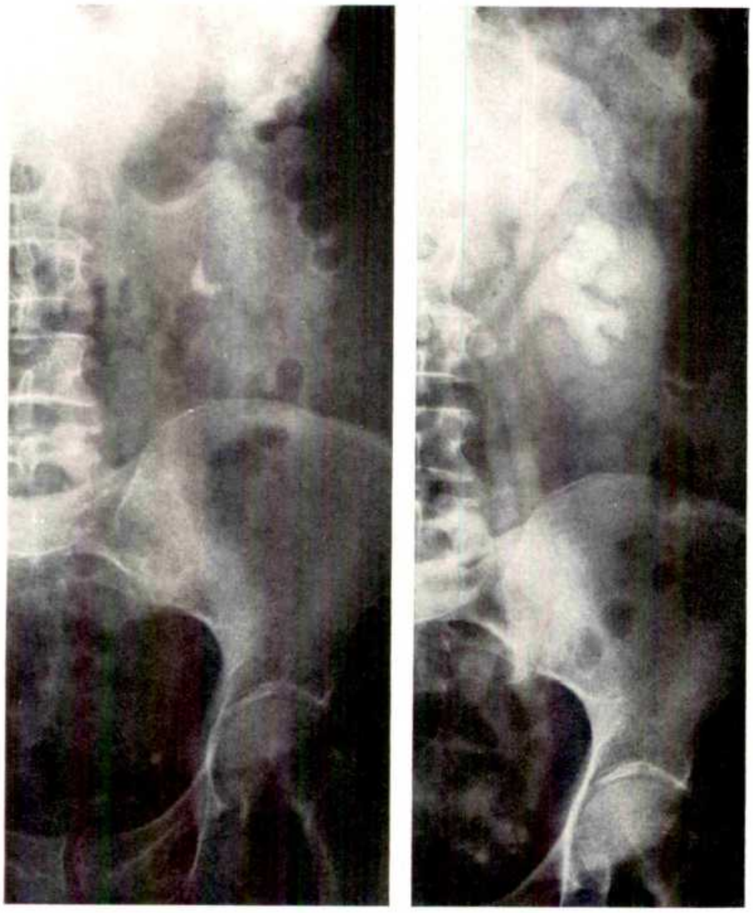
junction of a bifid ureter. The renal segment in which the stone formed, and its ureter, can be expected to remain exposed to the destructive effect of the calculous for a longer period than the other segment. The problem is exemplified in Figure 7.

Triplicated ureters are subject to calculous disease similar to that in duplicated ureters (Fig. 8).


A FIG. 7 B

58-year-old woman with left flank pain. A, Preliminary abdominal film: a calculous is seen in the left renal region; many smaller calcific densities appear in the pelvis. B, Delayed excretory urogram: one of the calcific densities is seen to be a stone in the common ureter of a bifid system, where it obstructs outflow. The renal calculous is seen to be in the lower renal segment.

The female patient with ureteral duplication may have an ectopic ureter opening into the urethra, vagina, or vulva, leading to urinary incontinence. If a stone blocks the ectopic ureter, the incontinence may temporarily cease during the presence of the symptoms of calculous disease. Transient cessation of incontinence may thus be a clue to calculous disease.

A counterpart of this situation may occur in the male. A stone may form in an ectopic ureter that opens in the prostatic urethra. Its presence may increase the obstruction caused by benign prostatic enlargement. We recently saw a 55-year-old man who went into acute urinary retention because a calculous in the ectopic ureter obstructed the prostatic urethra.

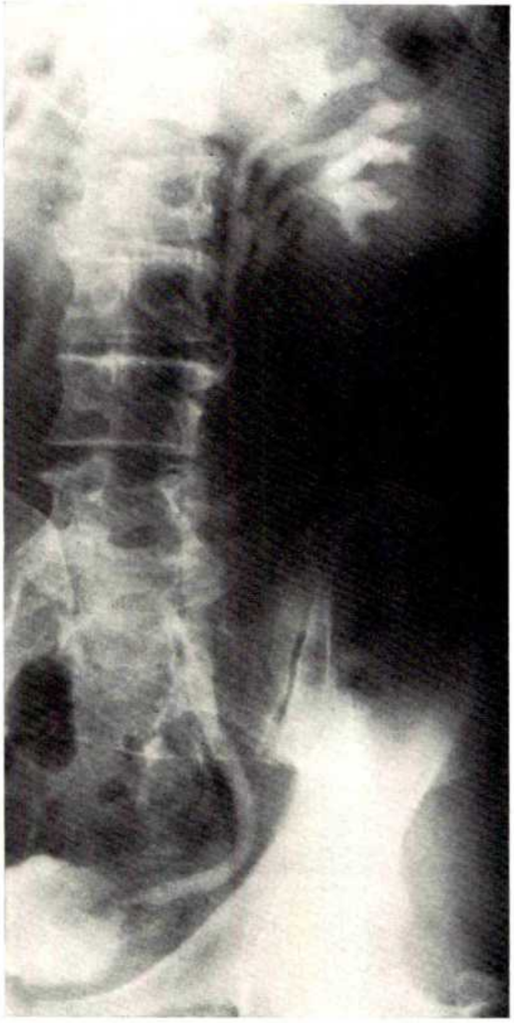


FIG. 8
A calculous at the lower end of a ureter which is triplicated as it reaches the kidney.

TREATMENT

Any meaningful discussion of calculous disease in ureteral duplication must emphasise the total management of the patient with this combination of afflictions. The individual patient's situation must be considered in detail and as a whole. Solution of his or her problem depends on knowledge of the individual's total urinary tract before surgical intervention. The recent advances in the surgical treatment of disease associated with ureteral duplication have been summarised elsewhere (Amar, 1968; and in press). Difficulties likely to be encountered are noted below.

If obstruction at the junction of a bifid ureter which has contributed to calculous disease is allowed to persist after removal or passage of the stone, calculous formation is prone to recur. Correction of obstruction at the junction is an integral part of the surgical treatment of the calculous disease (Fig. 2).

Where the stone is in the blind-ending limb of an incompletely duplicated ureter, the blind-ending limb containing the stone should be excised (Fig. 9).

Knowledge of the anatomy and vascular supply of the kidney in patients with duplicated ureters is important to the successful removal of a stone from either the upper or the lower renal segment. Duplicated renal arteries, which occur in only 20 per cent of persons with single ureters, are found in 50 per cent of patients with duplicated ureters (Boijsen, 1959). During the surgical procedure, injury must be avoided not only to the blood vessels, but also to the ipsilateral renal segment, its pelvis and ureter.

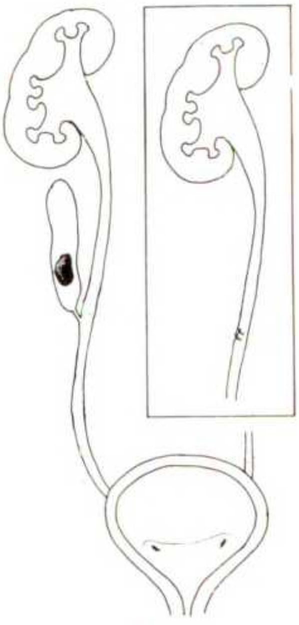
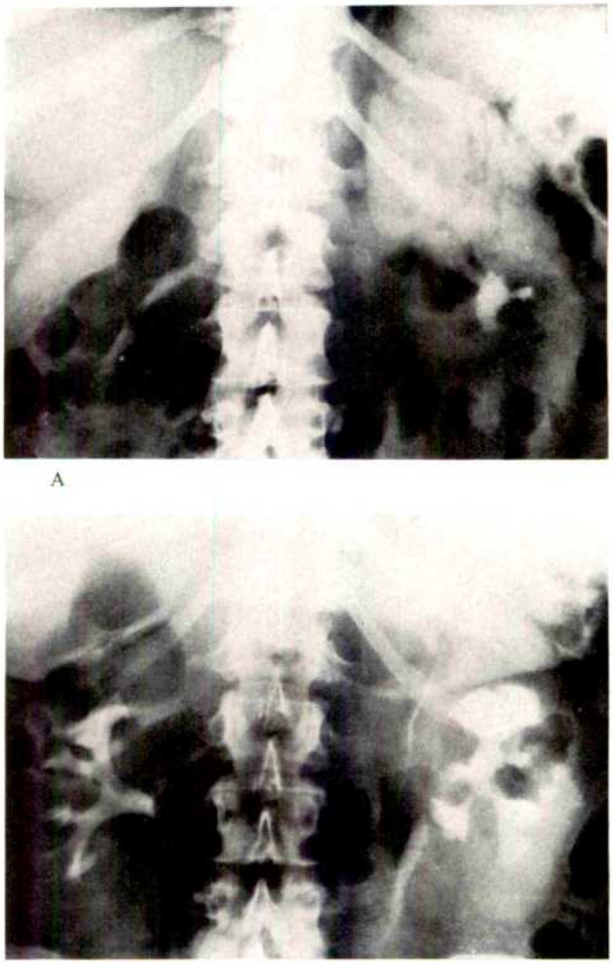


FIG. 9

Fig. 9.—Schema of calculous in the blind-ending ureter in incomplete ureteral duplication. The inset shows excision of the blind-ending ureter to prevent further calculous formation.



A

B

FIG. 10

Fig. 10.—42-year-old woman with chronic urinary tract infection and left flank pain. A, Preliminary film shows a branching calculous in the lower portion of the left kidney. B, Intravenous pyelogram: normal right kidney and caliceal structures. On the left there is ureteral duplication. The lower renal segment is intra-renal. Surgical removal of the branched renal calculous in the left renal segment was rather difficult because of the intra-renal position of the renal pelvis. (Courtesy of Dr Byron Olson.)

Removal of a staghorn calculous from a renal pelvis may be a difficult surgical procedure, especially when the renal pelvis is intra-renal (common in the upper renal segment) or when the renal segment is malrotated (as the lower renal segment frequently is). An example is shown in Figure 10.

Where a renal segment's function has been markedly impaired by stone and infection, sacrifice of the segment may be the best insurance against recurrence of calculous disease. If one is presented with a choice between sacrifice of the upper or the lower segment, it is important to preserve that which is less affected by chronic pyelonephritis and obstruction. When it appears that urine cannot be satisfactorily conducted from one renal segment by its own ureter, anastomotic procedures can be used to great advantage. Renal parenchyma can be preserved if the ureter or pelvis of the affected segment can be anastomosed to the unobstructed ipsilateral ureter or renal pelvis.

It is important to determine whether reflux is associated with ureteral duplication. If reflux persists after the removal of the stone, its correction by ureteral reimplantation may be essential to the eradication of infection in the involved renal segment, and thus to the prevention of further stone formation (Amar, 1972). Other methods of correction of reflux should also be considered, including ipsilateral uretero-ureterostomy or heminephro-ureterectomy.

Surgical correction of associated ureteral ectopia may be indicated.

Where stones are removed from a ureterocele associated with ureteral duplication, the ureterocele should also be removed, and the duplicate ureters should be reimplanted by an anti-reflux operation. If the ureter attached to the ureterocele is much dilated, one may need to remove it. Where the renal segment has salvageable parenchyma, its pelvis should be anastomosed to the ipsilateral lower renal pelvis. A renal segment that has little or no functioning tissue should be removed.

Calculous disease occurs at least as often in pregnant as in non-pregnant women, and pregnancy increases the risks associated with calculous disease (Amar, 1966). Ureteral duplication adds further complexities. The management of such patients requires careful consideration of all factors involved.

FOLLOW-UP

Every patient with ureteral duplication and calculous disease must be followed for an extended period. Problems may arise at any time in the future because of the anomaly, or because of factors arising from medical or surgical treatment rendered. One must determine with certainty that the treatment has been effective, and that difficulties relating to the duplication have been solved or are under control.

SUMMARY

The anatomical and physiological peculiarities that contribute to difficulty in the diagnosis and management of calculous disease associated with ureteral duplication are illustrated by case examples from the author's experience with 20 patients treated over the last 10 years. In addition to the removal of the calculous or calculi, management must include the surgical treatment of urinary tract disease associated with ureteral duplication. Such surgical treatment will help to prevent the recurrence of calculi in these patients. A prolonged period of follow-up is necessary.

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STRUCTURAL EVIDENCE IN SUPPORT OF AN URINARY TRACT PACEMAKER

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MUCH has been written on the control of ureteric activity and a review of this literature reveals a confusing, and often conflicting, state of knowledge on the subject. An observation about which there is general agreement, however, is that contraction waves normally begin in the upper part of the urinary tract. This fact has led to a quest for a possible pacemaker site in the region and both physiological and cinefluorographic techniques have been employed. On the basis of such evidence, some workers have considered the pelvicalyceal system to be of importance (Narath, 1951; Morales *et al.*, 1952; Mitsuya *et al.*, 1962; Kobayashi, 1964), whilst others, using similar techniques, have localised the " active " site to the pelvi-ureteric junction (Benjamin *et al.*, 1956; Shiratori and Kinoshita, 1961; Campbell, 1966; Weiss *et al.*, 1967). A number of other factors have been considered in relation to ureteric peristalsis and attempts made to assess their relative importance. In this context, the rôle played by autonomic nerves has been extensively studied and has proved particularly difficult to establish. This is not unexpected when one considers the widely differing reports on the structural arrangement of nerves in the urinary tract. Thus some observers (Duarte-Escalante *et al.*, 1969; El-Badawi and Schenk, 1969) have described ganglion cells widely distributed in the upper ureter, whilst others (Notley, 1968; Gosling, 1970*a*) believe that nerve cell bodies are absent from this region. It is hardly surprising, therefore, that the responses of the ureter to neuropharmacological experimentation are interpreted differently by different workers.

Strong evidence in support of a region acting as a pacemaker is that of relevant structural specialisation confined to that area. In the case of the urinary tract such " relevant specialisation " might be expected to involve either smooth muscle, or nerves, or both. Recently, anatomical (Gosling, 1970*b*; Gosling and Dixon, 1971) and pharmacological (Gosling and Waas, 1971) evidence of this kind has been reported, which indicates that the pelvicalyceal portion of the urinary tract acts as a pacemaker in the rabbit, rat and guinea-pig. These species possess a single calyx in direct continuity with the renal pelvis and anatomical evidence is lacking for a specialised arrangement in multicalyceal systems. With this in mind, the present study has re-examined the multicalyceal urinary tract of the pig and human using light and electron microscopic techniques.

Materials and Methods.—Normal human material was obtained either post-operatively from 5 nephrectomy specimens removed for renal neoplasia or from post-mortem preparations (10 specimens) provided the latter were obtained within 12 hours of death. Fresh pig tissues (7 specimens) were obtained from recently slaughtered animals. In all cases, portions of the minor calyces and adjacent renal parenchyma, major calyces, renal pelvis, pelvi-ureteric region and upper ureter were rapidly removed and processed either for light or electron microscopy.

Light Microscopy.—Material was placed on cryostat tissue holders, orientated into the required plane and quenched in isopentane cooled in liquid nitrogen. Each tissue holder was transferred to a cryostat maintained at −25°C and serial sections cut at 15-20 m. thickness. Some sections were placed on glass slides, fixed for 10 minutes in neutral 10 per cent formalin and then stained according to Masson's trichrome technique. These were then dehydrated by passing through ascending concentrations of ethyl alcohol, mounted and examined in a Vickers M41 photomicroscope. Adjacent sections to those prepared histologically were processed for tissue catecholamines using the method of Spriggs *et al.* (1966). Sections were picked up on coverslips and dehydrated over phosphorous pentoxide for not less than 1¼ hours. These were then transferred to vessels containing 6 g. of paraformaldehyde previously stored in an atmosphere of 70·4 per cent relative humidity. The vessels were sealed and heated at 80°C for 1¼ hours. Each section was then mounted in liquid paraffin and studied in a Zeiss photomicroscope fitted with a Wotan HBO 200W lamp, excitor filter BG 12/4 mm. and barrier filter GG 9/1 mm.

Electron Microscopy.—Small blocks of tissue were obtained from the appropriate region and fixed immediately in one of the following: (i) 1 per cent osmium tetroxide at 4°C in acetate veronal buffer at pH 7·3 for 1 hour (Palade, 1952); (ii) 5 per cent gluteraldehyde at 4°C in 0·1 M cacodylate buffer at pH 7·3 for 2 hours (Sabatini *et al.*, 1963) followed by fixation for ½ hour in buffered 1 per cent osmium tetroxide; (iii) 3 per cent potassium permanganate at 4°C in acetate veronal buffer at pH 7·3 for 2 hours (Richardson, 1966). After fixation the tissue was dehydrated in ascending concentrations of ethyl alcohol and embedded in TAAB epoxy resin with the aid of propylene oxide. Thin sections were cut using glass knives and an LKB Ultrotome III ultramicrotome, stained with alcoholic uranyl acetate (Watson, 1958) and lead citrate (Reynolds, 1963) and examined in a Philips EM300 electron microscope.

Results.—*Light Microscopy.*—Since the arrangement and distribution of tissues in the upper urinary tract of the pig and human were similar, the following results apply to both species. Two distinct types of smooth muscle were recognised, one of which was confined to the region of attachment of each minor calyx to the renal parenchyma. In this situation the muscle cells formed a meshwork of fibres (Fig. 1) each separated by small amounts of connective tissue. Discrete muscle bundles were absent and the arrangement was that of a continuous sheet made up of interlacing fibres (Fig. 3). The latter were elongated and appeared irregular in outline. When compared with muscle in the renal pelvis and ureter, these cells contained scant, pale-staining cytoplasm with long darkly stained nuclei. A number of similar cells extended a short distance away from the calyceal wall and were closely applied to the subjacent renal parenchyma (Figs. 1, 3). Numerous vessels were identified in this region some of which ran obliquely between the muscle cells to enter the renal substance. From this sheet of closely related muscle cells overlying the forniceal region, others ran into the minor calyceal wall proper. These long, thin, muscle cells were separated by large amounts of connective tissue as they were followed into the calyceal wall (Fig. 4). In this region, a gradual transition occurred in the arrangement and form of smooth muscle. The muscle coat gradually increased in thickness and discrete bundles of muscle cells could now be easily recognised (Fig. 5). In contrast with muscle cells further towards the kidney, those grouped into muscle bundles were relatively large, closely packed and intensely stained. This second type of cell arranged into well-defined bundles continued through the major calyces, renal pelvis and upper ureter. It must be stressed, however, that the type of muscle cell identified at the attachment of each minor calyx was continuous with the type further out in the calyceal wall. In the major calyces, renal pelvis and upper ureter, frequent connections were made between adjacent smooth muscle bundles resulting in the formation of a plexiform layer of smooth muscle (Fig. 6). Whilst separate layers of muscle were not identified, circularly directed bundles usually ran on the external aspect of those whose orientation was oblique or longitudinal. Special arrangements of smooth muscle suggestive of a sphincteric mechanism were not identified in any part of the upper urinary tract.

Fluorescence Microscopy.—By applying the specific histochemical technique for catecholamines to sections adjacent to those used for light microscopy, it proved possible to study the relationship of noradrenergic nerves to other structures in the upper urinary tract. The nerve terminal regions usually appeared as fine beaded threads on a dark background and were readily distinguished from autofluorescent structures by their characteristic yellow-green colour. At the attachment of each minor calyx to the renal parenchyma, numerous noradrenergic nerves were identified running in close relationship to the muscle cells in this region (Fig. 2). Whilst some

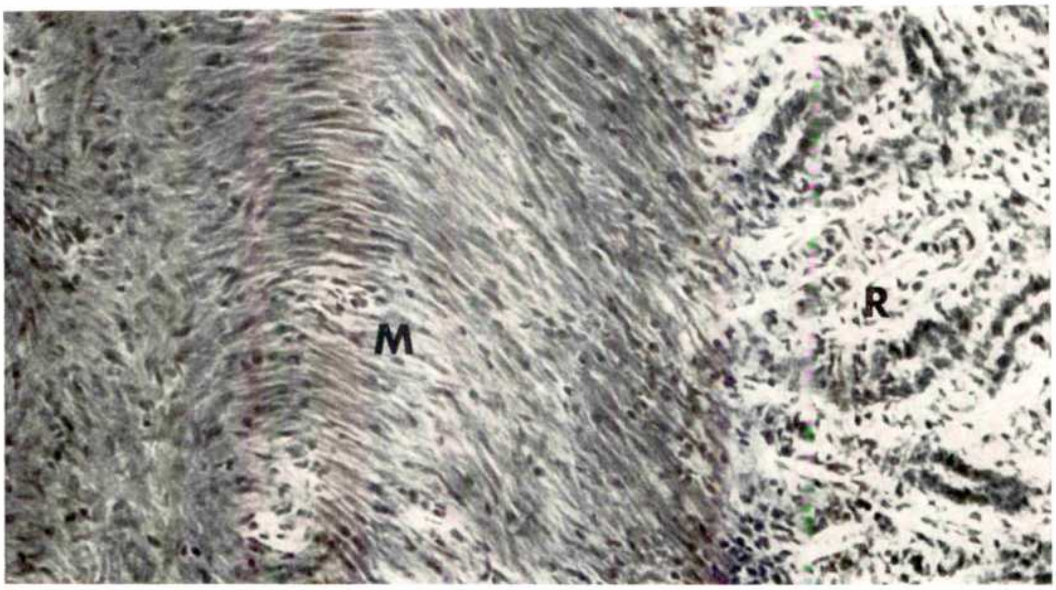

FIG. 1

An oblique section stained using Masson's trichrome technique, through the region of attachment of a minor calyx to the renal substance (R) in the pig. Muscle cells (M) are seen to be closely related to the kidney and form a meshwork of ill-defined fibres. × 200.

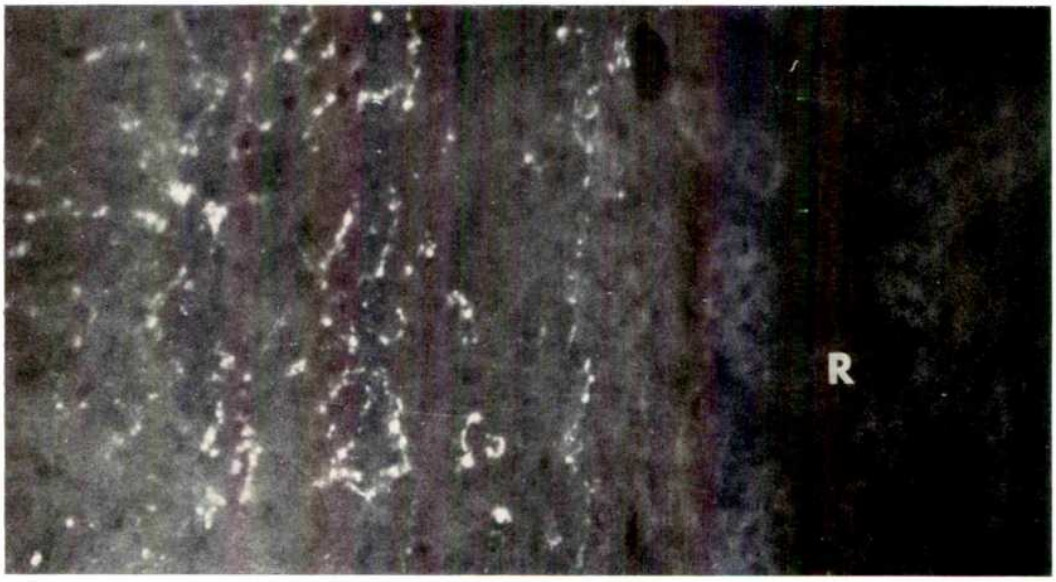

FIG. 2

Adjacent section to that illustrated in Fig. 1 but processed for tissue catecholamines. Noradrenergic nerve terminal regions (seen as white dots or lines against a dark background) are distributed throughout the meshwork of muscle cells. Note the absence of similar fibres from the adjacent renal parenchyma (R). × 200.

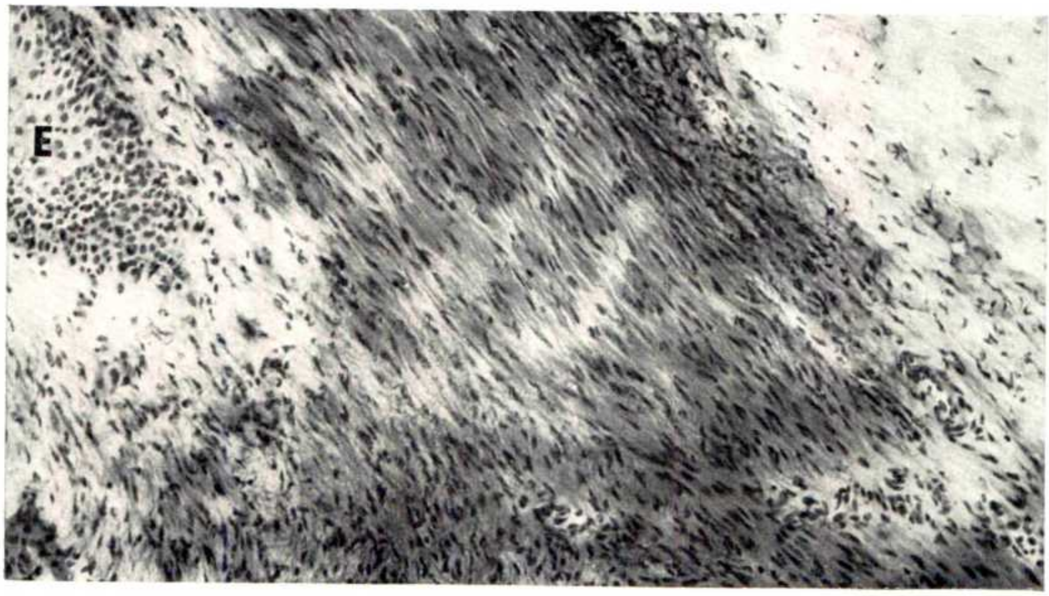

FIG. 3

Interlacing muscle fibres situated at the renal attachment of a minor calix in the human. Atypical muscle fibres extend out into the caliceal wall proper and overlie the epithelium (E) of the caliceal fornix. R = renal tubules. × 200.

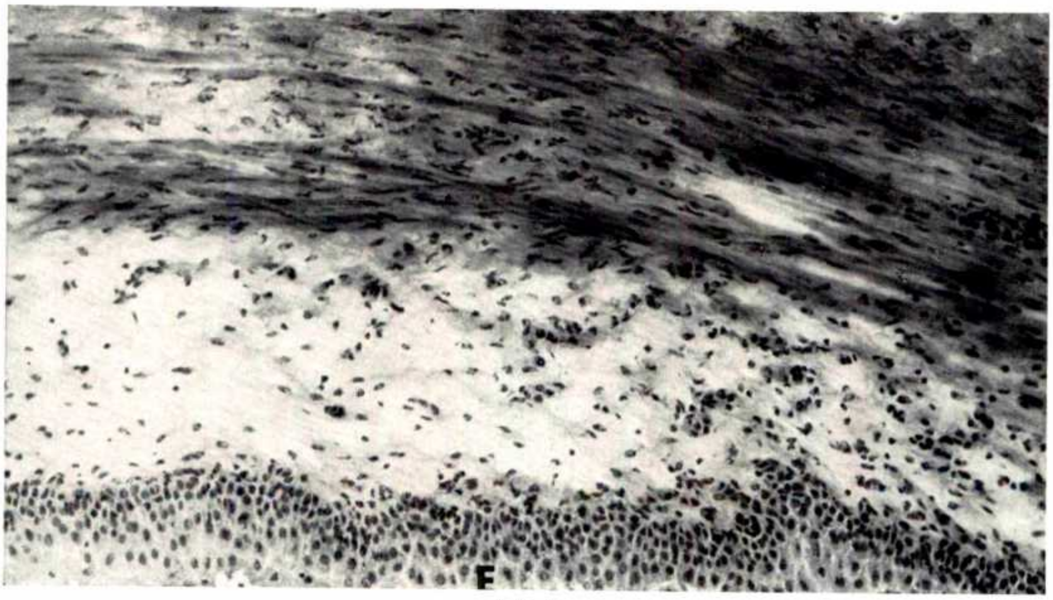

FIG. 4

Further out in the minor caliceal wall, the muscle cells are separated by quantities of connective tissue although muscle bundle formation is not yet apparent. Human material stained using Masson's trichrome technique. E = epithelial lining of the calyceal wall; P = renal papilla. × 150.

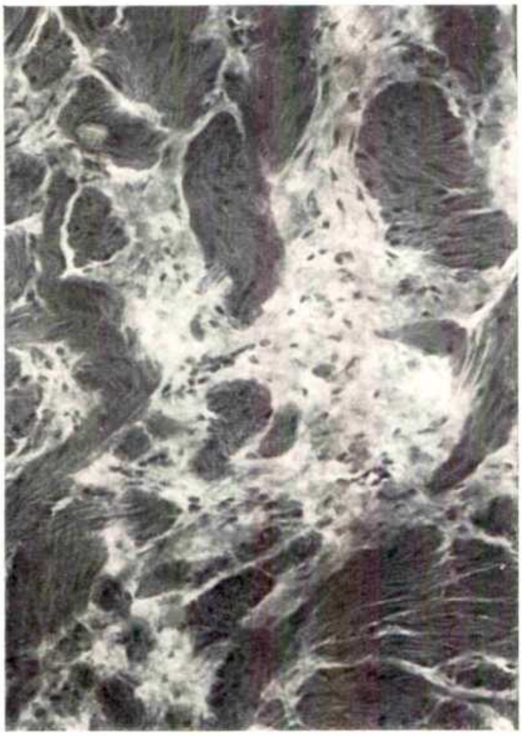

FIG. 5

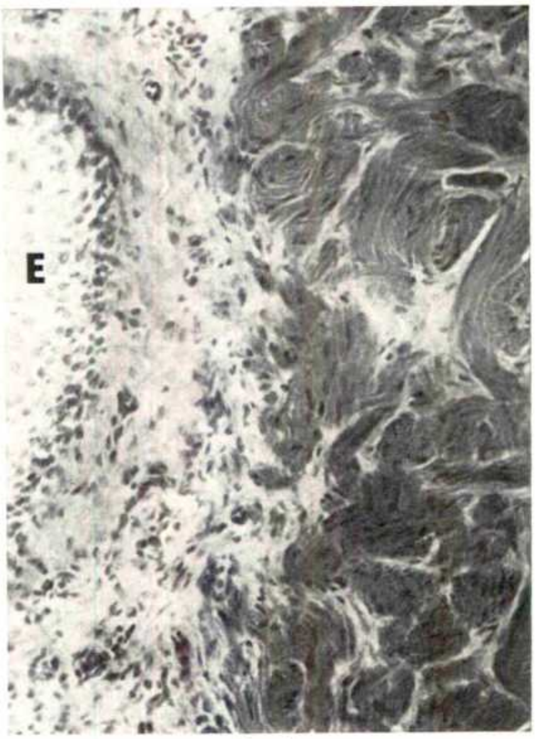

FIG. 6

Fig. 5.—In this oblique section of the muscle coat in the outer part of a minor calyx, muscle fibres are grouped together to form well-defined muscle bundles. Human material. (Compare with Fig. 1.) × 100.

Fig. 6.—The muscle coat in the wall of the renal pelvis and upper ureter is composed of muscle bundles running in a variety of directions. These are evident in this section through the human renal pelvis. E = epithelium. × 100.

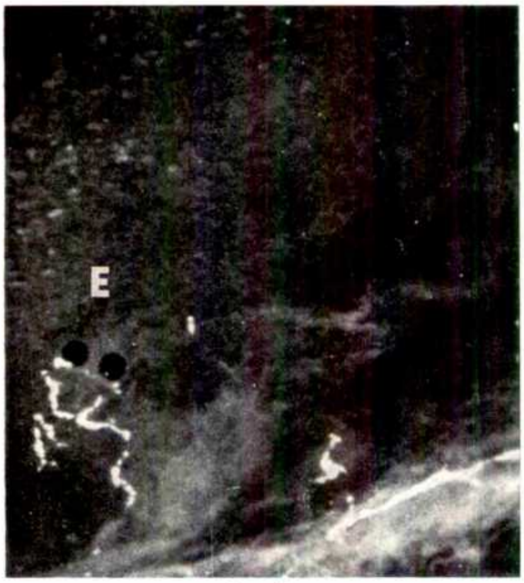

FIG. 7

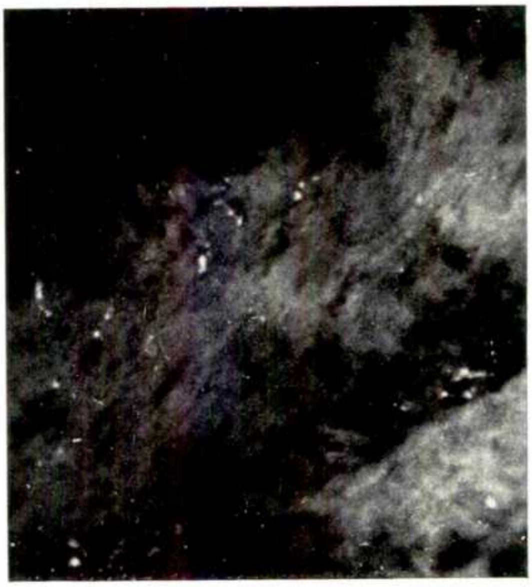

FIG. 8

Fig. 7.—A fluorescence preparation showing a few noradrenergic nerves in the submucosa one of which runs towards the base of the epithelium (E). Pig renal pelvis. × 250.

Fig. 8.—A section through the muscle coat of the pig ureter in which relatively few noradrenergic terminals can be seen amongst the smooth muscle bundles. (Compare with Fig. 2.) × 150.

of these nerves were undoubtedly related to vessels, the majority coursed through the muscle sheet unrelated to vascular structures. It is noteworthy that similar nerves were absent from the adjacent renal parenchyma.

As the muscle coat was followed into each minor calyx the density of associated noradrenergic nerves markedly decreased. A few terminal regions were related to muscle bundles but the major portion of the muscle coat was devoid of associated noradrenergic nerves (Fig. 7). Similar results were obtained when sections of the major calyces, renal pelvis and upper ureter were studied. Throughout the upper urinary tract, small submucosal arteries and arterioles were accompanied by networks of nerves lying in the adventitia of these vessels. In addition, occasional fine noradrenergic nerves were closely related to the basement membrane of the epithelium (Fig. 8) although intra-epithelial nerves were not identified. In all sections, neither fluorescing nerve cell bodies nor " chromaffin-like " cells were observed.

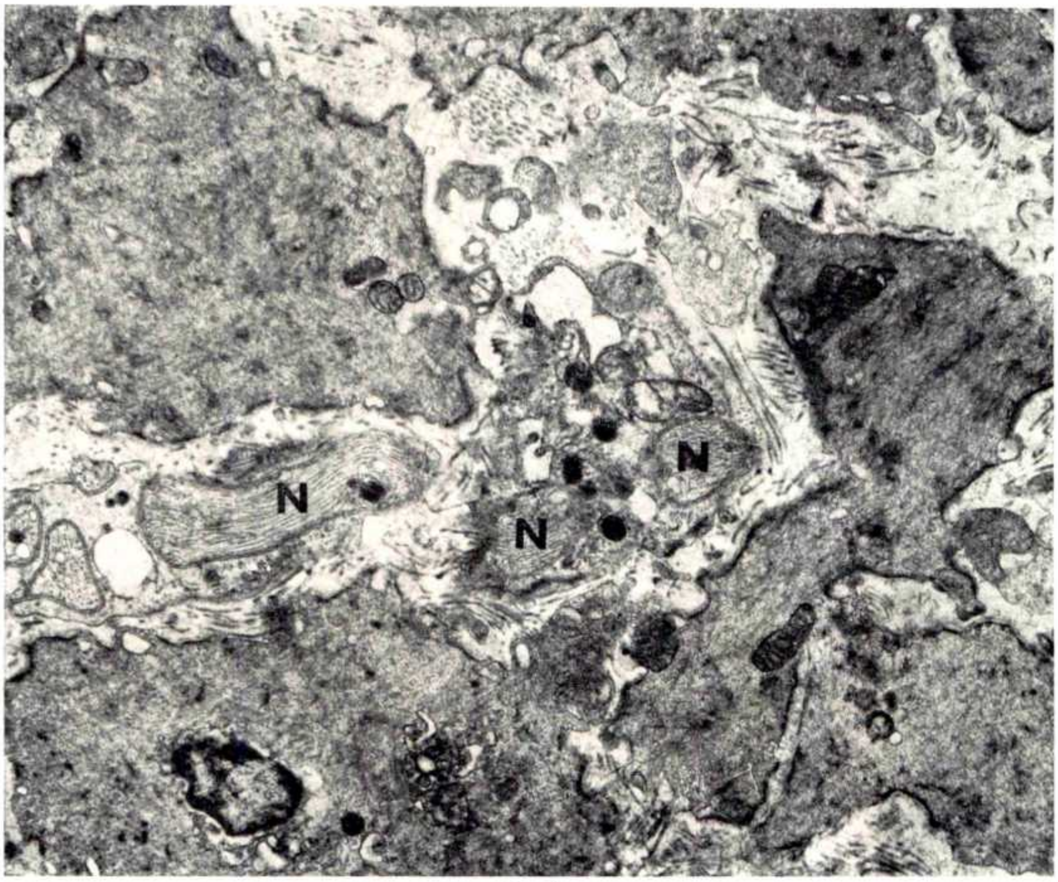

FIG. 9

An electron micrograph of irregularly shaped muscle cells adjacent to the renal tubules in the pig. Several nerve axons (N) lie among connective tissue between the cells. × 11,200.

Electron Microscopy.—As a result of relatively long delays prior to the fixation of human material, the fine structural detail of these tissues proved to be unsatisfactory. Consequently, the following results apply mainly to those specimens obtained from pig tissues. Sections from samples of the region of attachment of the minor calyces frequently included related portions of the renal parenchyma. The latter proved to be a useful guide in subsequent orientation of the tissue sections. Using the electron microscope, muscle cells in these preparations were identified in the connective tissue adjacent to the renal tubules. Since the muscle was not orientated in a particular direction, any given section included portions of cells cut in a variety of planes (Fig. 9). Irrespective of the plane of section, the majority of muscle cells displayed numerous outpouchings of the sarcolemma giving them an extremely irregular outline. A number of the cells were packed with thin dense filaments whilst in others, long bundles of filaments were interspersed between regions of granular reticulum. Many muscle cells contained regions of pale-staining cytoplasm in which were embedded numerous dense glycogen granules. In this region nerve bundles containing from 1 to 10 unmyelinated axons and their associated neurolemmal cells were regularly observed lying in connective tissue close to muscle cells. Some axons adjacent to these cells contained synaptic vesicles characteristic of those found in noradrenergic neuro-effector terminal regions (Fig. 10).

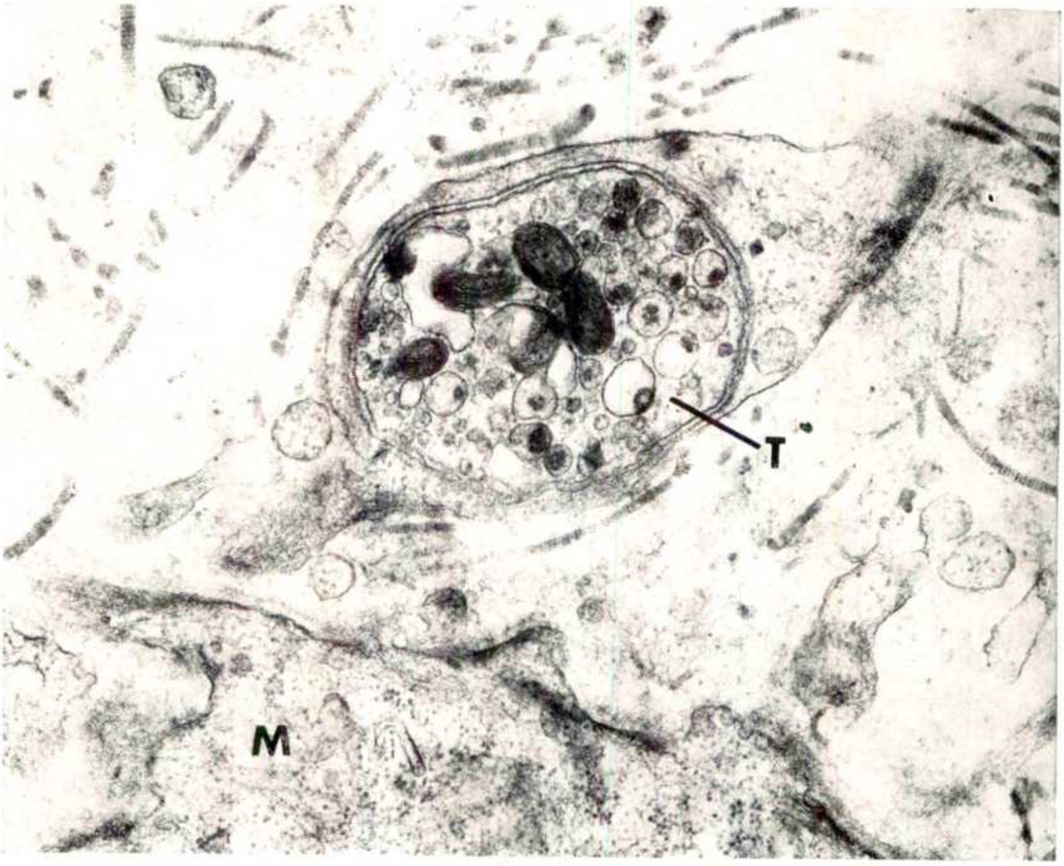

FIG. 10

A nerve terminal (T) in close association with an atypical muscle cell (M) close to the pig renal parenchyma. The axon contains several small mitochondria and synaptic vesicles many of which possess a dense core. × 33,000.

Tissue sections were also studied from the distal parts of minor calyces, the major calyces, the renal pelvis and the upper ureter. The fine structure of the muscle coat in these samples was similar although it differed markedly from that in sections of the calyceal attachment to the kidney. In these regions the muscle was arranged into numerous discrete branching bundles separated by amounts of connective tissue. Each bundle consisted of closely packed muscle cells running parallel to one another (Fig. 11). These relatively large cells were devoid of any atypical fine structural features and need not be further described. Finally, nerves were exceedingly scarce amongst the smooth muscle bundles—indeed they were completely absent from the majority of sections. Those nerves which were observed usually ran in the connective tissue between the muscle bundles and rarely contained organelles characteristic of nerve terminal regions.

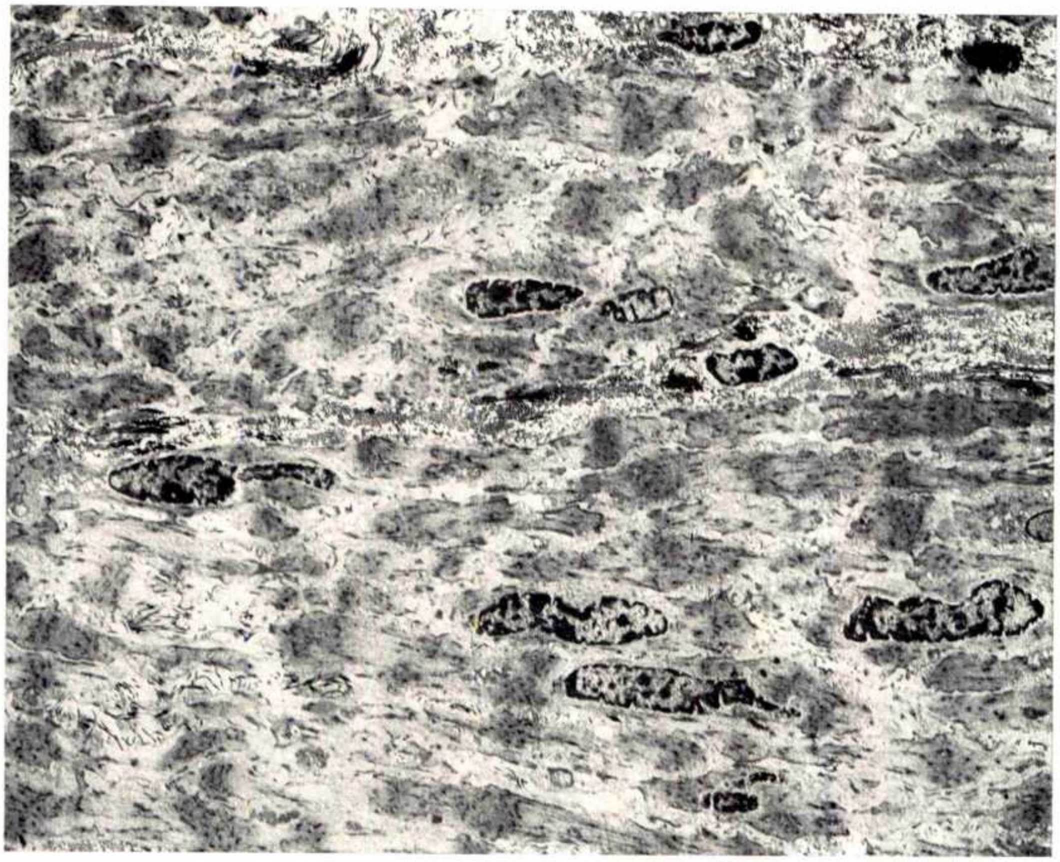

FIG. 11

A low-power electron micrograph of human ureteric smooth muscle cells. Note their compact arrangement and the absence of nerve fibres in this section. × 2,800.

DISCUSSION

The present investigation has demonstrated differences in the structure, arrangement and innervation of smooth muscle in the upper urinary tract of the pig and the human. Using light and electron microscopy, cells with characteristics unlike those in other regions were confined to a narrow zone at the renal attachment of each minor calyx. Recently, somewhat similar observations have been reported on the distribution of two types of smooth muscle in the proximal urinary tract in a number of animals each possessing a single calyx (Gosling, 1970*b*; Gosling and Dixon, 1971). Thus both unicalyceal and multicalyceal systems show localised structural modifications.

The functional significance of these observations is intriguing and worthy of further discussion. The location of smooth muscle close to the kidney raises the question of its possible effects upon the underlying renal parenchyma. Such a mechanism was proposed by earlier workers who considered the renal calyx to " milk " the renal papilla and thereby empty the collecting ducts of their contents (Henle, 1866; Muschat, 1926). In the present study, previously unrecorded modified smooth muscle was found surrounding only the base on each renal papilla. Thus, the reason for this specialisation cannot be explained in terms of an action on the papilla as a whole. Localised effects on the base of the papilla are equally unlikely when one considers the thin sheet of muscle cells in comparison with the relatively enormous amount of underlying renal substance. In keeping with this view, the paucity of myofilaments within these cells (when compared to others further out in the urinary tract) suggests that their contractility must be of secondary importance.

A number of vessels were observed near the renal attachment of each minor calyx, some of which ran through the muscle sheet to enter the adjacent renal parenchyma. Possible effects may therefore be exerted upon these vessels by the smooth muscle confined to the region. This explanation for its presence seems improbable since the majority of these vessels already possessed typical smooth muscle cells confined to the media in a manner similar to that of other intra-renal vessels. Furthermore, the electron microscope has shown that relatively large areas of modified smooth muscle were unrelated to vascular structures. It therefore seems reasonable to propose that the majority of vessels in this region simply run through the muscle without being directly influenced by it.

The most likely explanation for the present observations is in accord with the concept of an urinary tract pacemaker. Ureteric peristalsis normally proceeds in a direction towards the bladder indicating that contraction waves arise in the proximal part of the urinary tract. Both electrophysiological and cinefluorographic methods have been employed in attempts to locate such a region. These studies, however, lacked anatomical evidence of cellular specialisation which would have substantially strengthened the case for a pacemaker region or regions. Whilst localised muscle thickenings have not been observed in the present study, structurally different smooth muscle was confined to a region ideally positioned to initiate peristaltic activity, the subsequent direction of which would be towards the bladder. The continuity of this muscle with that further out in the urinary tract indicates that activity originating in this region could be propagated to the remainder—the close apposition between adjacent cells provides electron microscopic evidence for electrotonic spread of the impulse from one muscle cell to another.

The renal attachment of each minor calyx has been found to include modified smooth muscle cells. Thus, contraction of the renal pelvis may well result from summation of activity from all the minor calyces. The location and number of these regions may explain why peristaltic activity continues after partial nephrectomy or renal transplantation since at least some of the " pacemaker " sites would remain intact or be transplanted. The rich adrenergic innervation of these regions is also worthy of consideration. Physiological studies on the isolated calyceal wall of both unicalyceal and multicalyceal animals (Muschat, 1929; Finberg and Peart, 1970; Gosling and Waas, 1971) have shown these regions to possess spontaneous activity. In addition, both the rate and amplitude of these spontaneous contractions was increased by the addition of exogenous noradrenaline. These results indicate that the noradrenaline-containing nerves presently identified may well subserve an excitatory function to calyceal smooth muscle. Whilst nerves are probably not essential for spontaneous activity, their function may be to modify smooth muscle contractility and to integrate and co-ordinate contractions arising in a number of separate minor calyces.

In conclusion, the results of this study allow speculation on the ætiology of hydronephrosis of the type where apparent dysfunction in the region of the pelvi-ureteric junction occurs in the absence of any recognised structural cause. On the basis of the present hypothesis, contraction waves normally originating in the minor calyces pass across the renal pelvis in an integrated fashion. These peristaltic waves continue through the pelvi-ureteric junction down the ureter towards the bladder. In such a system, if calyceal dysfunction occurred, contraction waves throughout the remainder would also be affected resulting in an apparent barrier to urine flow at the narrowest part of the upper urinary tract—namely the pelvi-ureteric junction. When once the condition has been established, additional mechanical factors (*e.g.* kinking of the pelvi-ureteric junction) could impede still further the passage of a bolus of urine. It may well be that pyeloplasty ameliorates these secondary factors (where such exist) without altering the primary defect which exists in regions proximal to that usually regarded as the offending segment. Whilst many questions remain unanswered, the present study helps to focus attention on an area where future research may further our knowledge of the dynamics of the urinary tract.

SUMMARY

Using light and electron microscopic techniques, the arrangement and distribution of smooth muscle and of noradrenergic nerves has been examined in the multicalyceal upper urinary tracts of the pig and human. Smooth muscle confined to the renal attachment of each minor calyx appeared structurally different from that which extended throughout the major calyces, renal pelvis and upper ureter. The two types of muscle, however, were in continuity with one another. A relatively rich supply of noradrenergic nerves was also identified in relation to these modified smooth muscle cells adjacent to the renal parenchyma; very few similar nerves were seen amongst the muscle bundles in the remainder of the upper urinary tract. In conjunction with other studies, it is proposed that these observations are best interpreted as structural evidence for a pacemaker system localised to the proximal part of the urinary tract in these species.

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CARCINOMA OF THE BILHARZIAL BLADDER IN EGYPT

Clinical and Pathological Features

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The relationship between bilharziasis and carcinoma of the bladder was first reported by Fergusson (1911). Since then many valuable contributions have been added. Makar (1955), El Sebai (1961), and Abdel Tawab (1966), from Egypt emphasised this relationship. Similar conclusions were also reported from Rhodesia (Gelfand *et al.*, 1967), and from Iraq (Halawani *et al.*, 1970).

The aim of this study is to present the particular clinical and pathological aspects of carcinoma of the bilharzial bladder as seen in Egypt. The work is based on data collected from 304 cases with bladder cancer examined at the Department of Urology, Mansoura University Hospital, and the Institute of Cancer, Cairo, during 3 consecutive years (1967-1970).

Age and Sex Distribution.—Figure 1 is a diagrammatic representation of the age and sex distribution of 304 patients with carcinoma of the bladder. The male to female ratio was 4 : 1. The average age was 46·7 years for the males, 44·6 for the females, and 46·3 for the whole group.

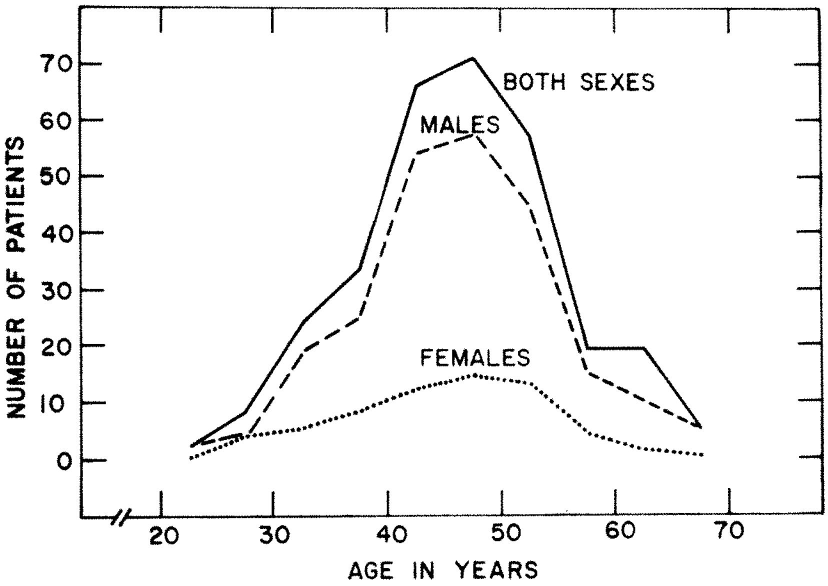

Fig. 1

Age and sex distribution of 304 cases of bladder cancer.

Clinical Presentation.—A summary of the main clinical presentations is given in Table I. Cystitis symptoms, painful micturition, frequency and hæmaturia were the most frequent clinical presentations.

Staging.—The T.N.M. staging system advocated by the U.I.C.C.[1] was applied. Bimanual examination of the empty bladder under anæsthesia, cystoscopy and biopsy were considered mandatory in determining the clinical stage. This was later checked in the course of pathological examination.

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[1] Union International Contre le Cancerum, Geneva, 1967. The sub-committee of clinical stage classification and applied statistics. Malignant tumours of the urinary bladder: clinical stage classification and presentation of results.

Seventy-five cases (24·6 per cent) were considered clinically inoperable. Table II represents the staging of 229 cases as pathologically determined. The majority of cases (68·2 per cent) revealed deep infiltration of muscles or perivesical adipose tissue (P3). The pre-operative estimation of the extent of the disease was compared with the pathological one in 135 cases to establish the degree of clinical error (Table III). The over-all error in clinical staging was 37·2 per cent and was highest at the T2 stage (75·6 per cent). In the majority of cases the error was due to clinical under-estimation of the extent of the disease.

TABLE I

Presenting Symptoms in 304 Patients with Carcinoma of the Bladder

Symptoms	No. of Cases	Percentage
Burning micturition . . .	140	65·1
Frequency	138	64·2
Hæmaturia . . .	103	47·9
Necroturia	84	39·1
Suprapubic pain . . .	51	23·7
Pyuria	50	23·3
Difficulty	35	16·3
Renal pain	29	13·5
Retention	7	3·3

TABLE II

Pathological Staging (U.I.C.C.) of Carcinoma of the Bilharzial Bladder

Stage	Number	Percentage
P1	8	3·9
P2	35	15·1
P3	157	68·2
P4	29	12·8
Total	229	

TABLE III

Error in Clinical Staging (T.N.M.) as Verified by Pathological Staging in 135 Cases

Clinical Stage	No. of Cases	Pathological			
		P1	P2	P3	P4
T1	...	...	...	...	...
T2	37	1	9	27	...
T3	96	...	6	74	16
T4	2	...	...	...	2

Total clinical error:	50 cases	(37·2 per cent)
Error due to understaging:	43 cases	(31·8 per cent)

TABLE IV

Site of Origin

Site	Number	Percentage
Posterior wall . .	102	44·6
Anterior wall . .	36	15·7
Lateral walls . .	33	14·4
Vault	25	10·8
Trigone . . .	13	5·7
Multicentric . . .	20	8·8
Total . . .	229	

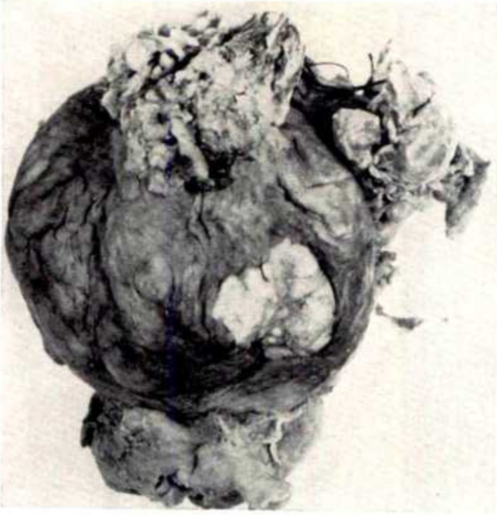

FIG. 2

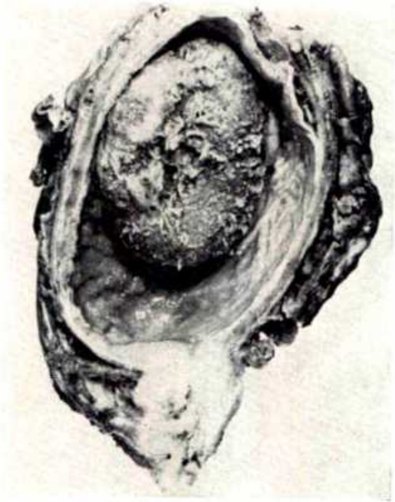

FIG. 3

Fig. 2.—Multicentric bladder tumours.
Fig. 3.—Nodular fungating tumour, lateral wall of bladder.

TABLE V

Gross Type of Carcinoma

Type	Number	Percentage
Nodular fungating .	157	68·5
Ulcerative . . .	58	26·5
Papillary . . .	9	3·6
Fibrillary . . .	5	2·3
Total . . .	229	

Table IV presents the site of origin of 229 cases of bladder cancers. The posterior wall was the commonest site of involvement (44·6 per cent), the trigone was the least (5·7 per cent). Multicentric tumours (Fig. 2) with involvement of more than one wall were present in 8·8 per cent of cases.

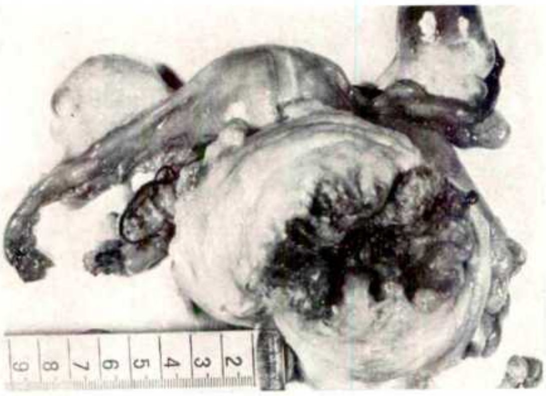

FIG. 4
Malignant ulcer, posterior bladder wall, invading vagina.

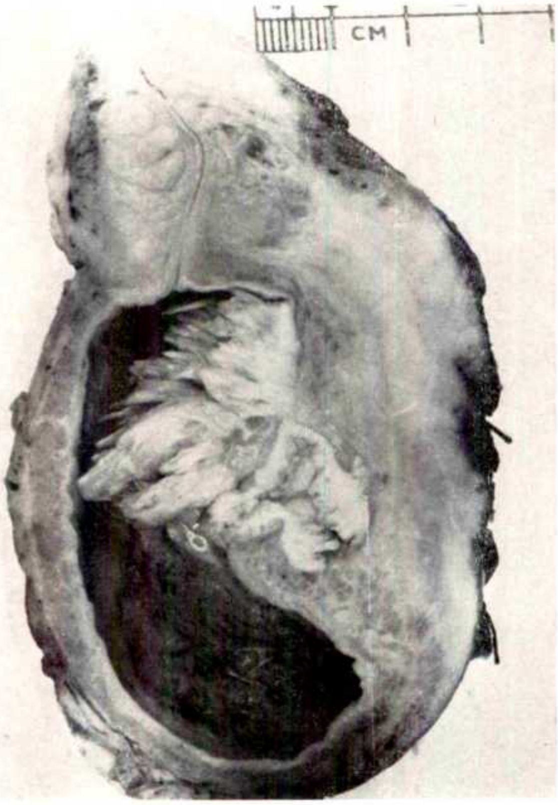

FIG. 5
Fibrillary tumour.

The gross morphological pattern of the tumours examined is given in Table V. Nodular fungating tumours (Fig. 3) are the commonest (68·5 per cent). Malignant ulcers (Fig. 4) constitute 26·5 per cent of cases. Papillary tumours are uncommon (3.6 per cent). A rare form which assumed a fibrillary appearance (Fig. 5) was present in 2·3 per cent of cases. Keratinised white masses were projecting from the surface of the growth like a tuft of hair.

Tumour Histology and Grade (Table VI).—Squamous cell carcinoma accounts for 66·7 per cent of cases. Of these 47 per cent were of the well differentiated variety (Fig. 6), 40 per cent were of Grade II tumours (Fig. 7), and 12 per cent only were of the poorly differentiated type (Fig. 8).

TABLE VI

Tumour Histology and Grade

Type	Grade						Total	
	I		II		III			
	No.	%	No.	%	No.	%	No.	%
Squamous	72	47·2	61	40·5	19	12·2	152	66·7
Transitional	4	7·7	17	30·7	33	61·5	54	23·4
Adenocarcinoma	3	16·7	11	55·6	5	27·7	19	8·1
Unclassified	...	...	...	...	4	100	4	1·8
Total	79	34·6	89	38·7	61	26·5	229	...

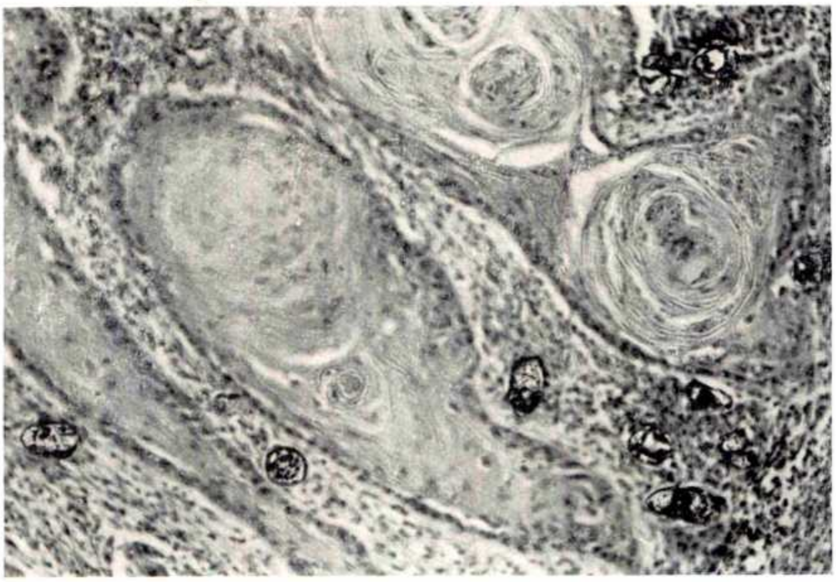

FIG. 6

Squamous cell carcinoma, Grade I. × 100.

Transitional cell carcinoma represents 23·4 per cent of cases only. This type may undergo squamous metaplasia (Fig. 9), a condition which should be distinguished from genuine squamous cell tumours.

Adenocarcinoma (Fig. 10) is uncommon and constitutes 8 per cent of the cases only.

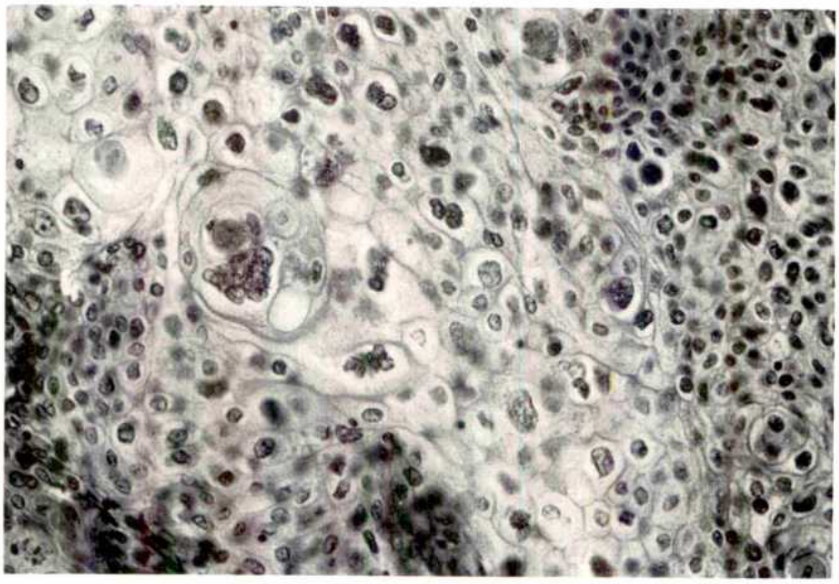

FIG. 7
Squamous cell carcinoma, Grade II. × 250.

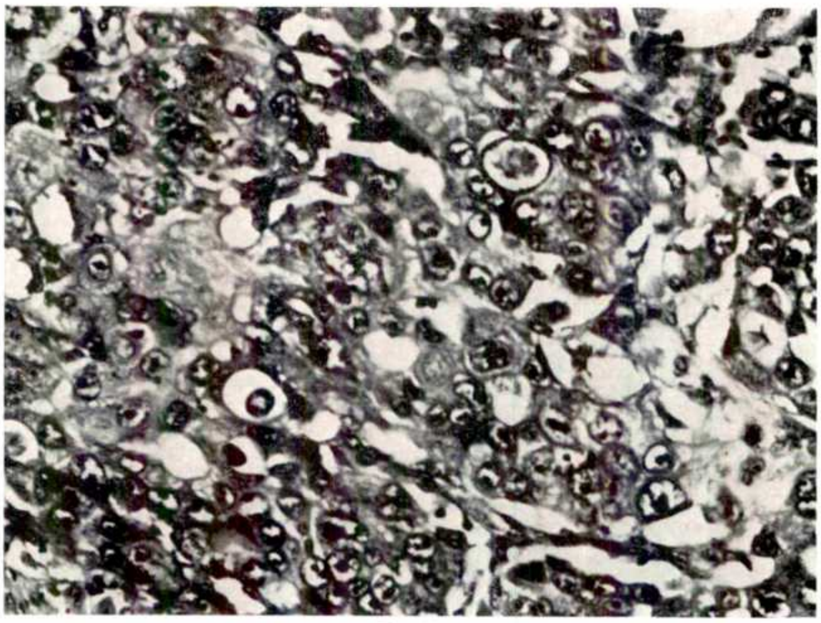

FIG. 8
Squamous cell carcinoma, Grade III. × 250.

Lymph node involvement.—Of the 229 cases examined, the regional lymph nodes were the seat of metastatic deposits in 34, an incidence of 15 per cent. Of these metastases involved one node in 14/34, and more than one in 20/34 of cases. Evidence of capsular infiltration could be demonstrated in 9/34 of the cases.

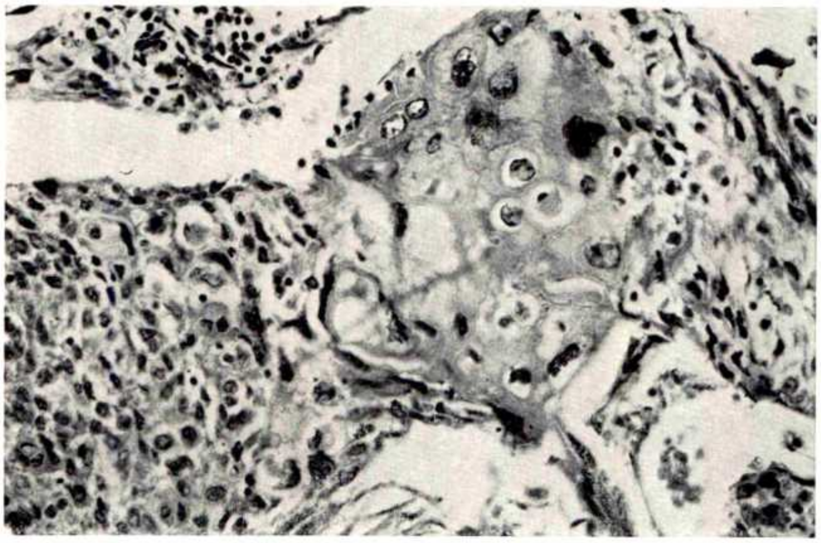

FIG. 9
Transitional cell carcinoma, Grade III, with squamous metaplasia. × 250.

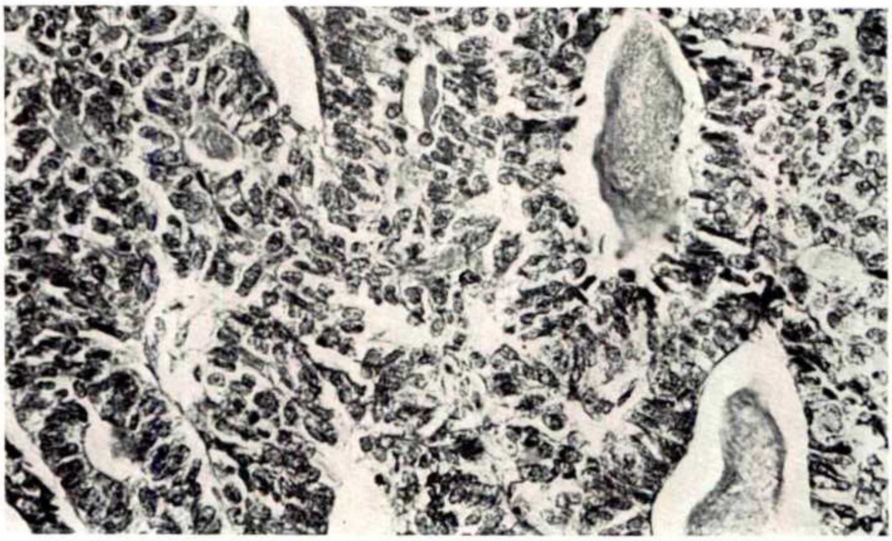

FIG. 10
Adeno-carcinoma. × 250.

The incidence of lymph node involvement was correlated to the tumour stage (Table VII), to the tumour histology (Table VIII) and to the tumour grade (Table IX). A statistically significant relationship could be revealed between the incidence of lymph node involvement and the tumour stage (especially at the P4 stage), and the tumour grade. However, a relationship between lymph node involvement and the histological type of tumour proved to be insignificant.

TABLE VII

Relationship between Lymph Node Involvement and Pathological Stage of the Carcinoma

Stage	Negative Nodes		Positive Nodes		Total	
	No.	%	No.	%	No.	%
P1	7	87·5	1	12·5	8	3·6
P2	32	90·9	3	9·1	35	14·8
P3	136	86·3	21	13·7	157	68·7
P4	20	68·9	9	31·1	29	12·9
Total	195	84·8	34	15·2	229	...

TABLE VIII

Relationship between Lymph Node Involvement and Histological Type of Carcinoma

Histological Type	Negative Nodes		Positive Nodes		Total	
	No.	%	No.	%	No.	%
Squamous . .	130	85·3	22	14·7	152	67·1
Transitional . .	47	86·6	7	13·2	54	22·6
Adenocarcinoma .	15	80·9	4	19·1	19	8·7
Unclassified . .	3	...	1	...	4	1·7
Total . .	195	84·9	34	15·1	229	...

TABLE IX

Relationship between Lymph Node Involvement and Grades of Carcinoma

Grade	Negative Nodes		Positive Nodes		Total	
	No.	%	No.	%	No.	%
I	73	92·5	6	7·5	79	34·6
II	73	82·0	16	18·0	89	38·5
III	49	80·6	12	19·4	61	26·9
Total	195	85·3	34	14·7	229	...

DISCUSSION

The average age incidence of 46·7 years is definitely much lower than figures reported for non-bilharzial cases. Payne (1959) gave an average age incidence of 63·5 years, with only 12 per cent of cases under the age of 50. Whitmore's (1962) figure was 58 years for a series of cases treated by radical cystectomy. Miller, Mitchell and Brown (1969) reported that the maximum incidence was in the seventh decade.

The male to female ratio of 4 : 1 can be explained by the fact that men working in the fields are at a higher risk of repeated infestations by the parasite.

The over-all error in clinical staging in this series was 37·2 per cent, with a tendency to under-estimate the extent of the disease in most cases. Whitmore (1962) gave a lower incidence of clinical error (22·7 per cent). On the other hand, Marshall (1952) and Kenny *et al.* (1970) gave a higher incidence (36·7 and 56 per cent respectively). Various factors could contribute to the tendency towards underestimation in this series:

1. Certain difficult sites for palpation, *e.g.*, tumours of the vault and anterior wall.
2. Inaccessibility of the regional lymph nodes for clinical assessment.
3. Endoscopic biopsy was only taken to establish the diagnosis and not to evaluate the depth of muscular infiltration due to the high risk of bladder perforation when dealing with advanced tumours.

When they were first examined, 25 per cent of the cases were considered inoperable. The late presentation of the majority of cases could be explained by the fact that the symptoms of simple bilharzial cystitis and malignant cystitis are similar. A considerable amount of time is thus lost before the patient can appreciate that qualitative changes in his symptoms warrant seeking serious medical advice.

The majority of tumours in this series were advanced with deep muscle infiltration in 68·2 per cent of cases. Extravesical spread was observed on 42 occasions in 29 cases (12·8 per cent). The prostate was involved in 5·6 per cent of cases only, as compared with the 50 per cent figure in non-bilharzial cancer (Melicow, 1955). This can be attributed to the fact that the trigone is a rare site of origin for tumours in the bilharzial bladder (5·7 per cent). On the other hand the trigone is a common site of involvement in non-bilharzial tumours; Mostofi (1956) gave a figure of 21 per cent. The rarity of involvement of the trigone in the bilharzial bladder corresponds with the finding that squamous metaplasia rarely affects this site (El Sebai, 1961).

The majority of bilharzial bladder cancers are of the nodular fungating variety in contrast to the overwhelming majority of papillary tumours in non-bilharzial cases. However, the preponderance of true squamous cell carcinoma is the most striking feature and stands in contradistinction to the well known fact that transitional cell tumours constitute most of the cases in non-bilharzial bladder cancers. Payne (1959) records 962 cases of bladder tumours of which 92·5 per cent were transitional.

Most of the squamous cell tumours are of low grade, characterised by the presence of cell nests and excess of keratin formation. As a result these cases are resistant to irradiation, and radical surgery provides the only chances for cure.

Finally, statistical correlations of results in this study revealed that advanced stages and high-grade tumours are associated with a greater chance of lymph node involvement and logically with higher incidence of recurrences. These facts are in agreement with those of Jewett (1946) and Baker (1955) in non-bilharzial bladder tumours.

SUMMARY

Carcinoma of the bilharzial bladder in Egypt is a special entity. The disease represents certain particular clinical and pathological features. In this series 304 cases with carcinoma of the bilharzial bladder were presented. The average age for the group was 46·7 years, with a male to female ratio of 4 : 1. When first seen 25 per cent of cases were inoperable. Nodular fungating tumours accounted for 68 per cent of cases. Histologically, most of the cases (66·7 per cent) were of the squamous cell type. The regional lymph nodes were involved in 14 per cent of cases.

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BONE AND CARTILAGE IN MALIGNANT TUMOURS OF THE URINARY BLADDER

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Bone and cartilage are rarely found in primary tumours of the urinary bladder but the problem raised by their histogenesis is an interesting one. Since Pang (1958) published 5 cases and reviewed 15 others reported previously, 9 cases of such tumours have appeared in the literature (Collins and Curran, 1959; Friedman and Ash, 1959; Frühling *et al.*, 1959; Nicolai and Spjut, 1959; Mioduszewska and Stapor, 1962; Kikuchi *et al.*, 1965; Theodossiou and Davillas, 1970). This paper reports 5 new cases and attempts to explain the presence of bone or cartilage in these tumours.

CASE REPORTS

The following 5 cases were found on reviewing 968 surgical specimens of tumours of urinary bladder examined in the Department of Pathology of the University of Athens.

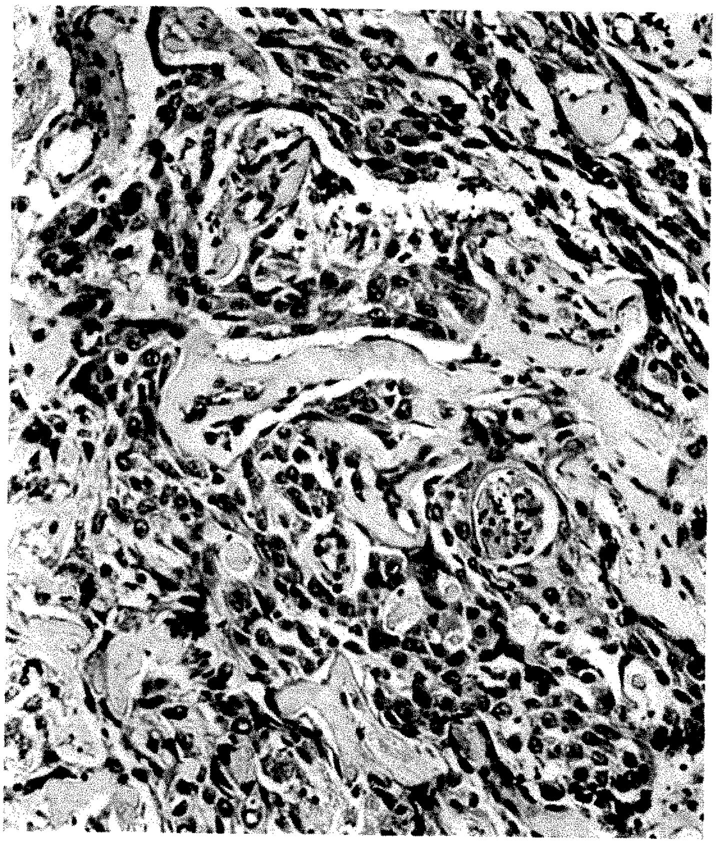

Fig. 1

Case 1, Bundles of osteoid in relation to carcinomatous clumps. Hæmatoxylin and eosin. × 140.

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Case 1.—A man aged 65 was admitted to hospital due to the onset of severe hæmaturia. A cystoscopy was attempted but, as the bladder could not be visualised, a laparotomy was performed. The bladder was enlarged and cystotomy revealed a large solid tumour infiltrating the right side of the bladder wall; on the left side the tumour had a papillary pattern. It was felt that cystectomy would not be worth while; biopsies were taken from both sides of the tumour. Radiotherapy was given but the patient died of pyelonephritis 3 months later. An autopsy was not performed.

The specimen from the papillary area has the typical appearance of a well differentiated papillary transitional cell carcinoma, showing superficial infiltration but not extending into the muscular layer.

The solid area has a slightly different pattern; the appearances are those of a poorly differentiated transitional cell carcinoma. In some areas there is squamous metaplasia and in others the tumour tends to be undifferentiated with multinucleated tumour giant cells. Within the stroma of these undifferentiated areas and in association with the clumps of carcinoma cells the stroma is arranged in bands of hyalinised connective tissue showing eosinophilic staining and containing wide blood vessels but few cells. The appearance is that of osteoid formation within the connective tissue but without mineralisation and only focal calcification (Fig. 1).

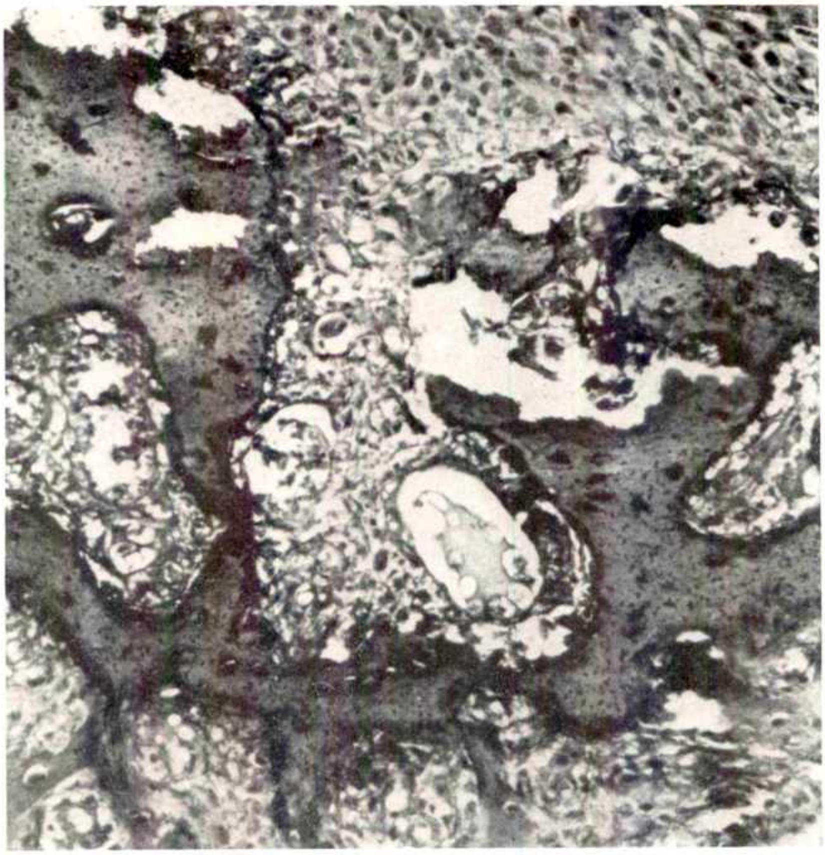

FIG. 2

Case 2, Bone trabeculæ with marrow-like spaces. H. &. E. × 140.

Case 2.—A man aged 56 was admitted to the hospital with severe hæmaturia. Cystoscopy revealed a hard solid tumour of the bladder which was biopsied. The patient refused any further treatment and left the hospital; we were unable to follow up the case.

Histology of the specimen shows the appearance of a moderately well differentiated transitional cell carcinoma. In some areas the tumour has a papillary pattern, in others the cells tend to be squamous but without keratin formation.

Within the stroma of the tumour there are several trabeculæ of bone most of which are calcified but no osteoblasts are visible. Within some of these bony trabeculæ there are spaces containing fat, reticulum and capillaries, a pattern which mimics the stroma of bone marrow but without hæmopoietic elements (Fig. 2). Chronic inflammatory cells are also present within the stroma.

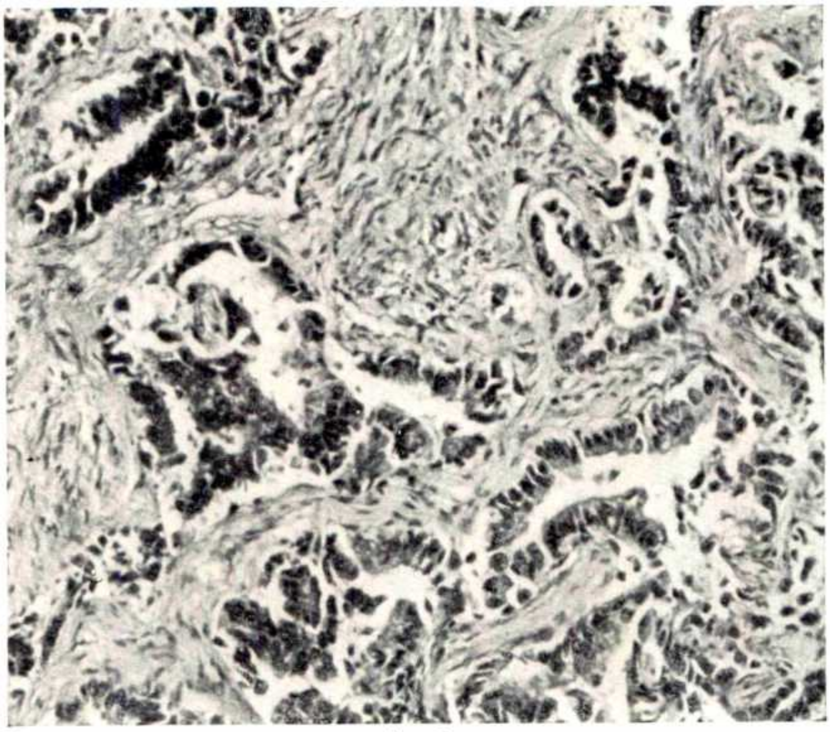

FIG. 3

Case 3, Carcinomatous clumps. H. & E. × 140.

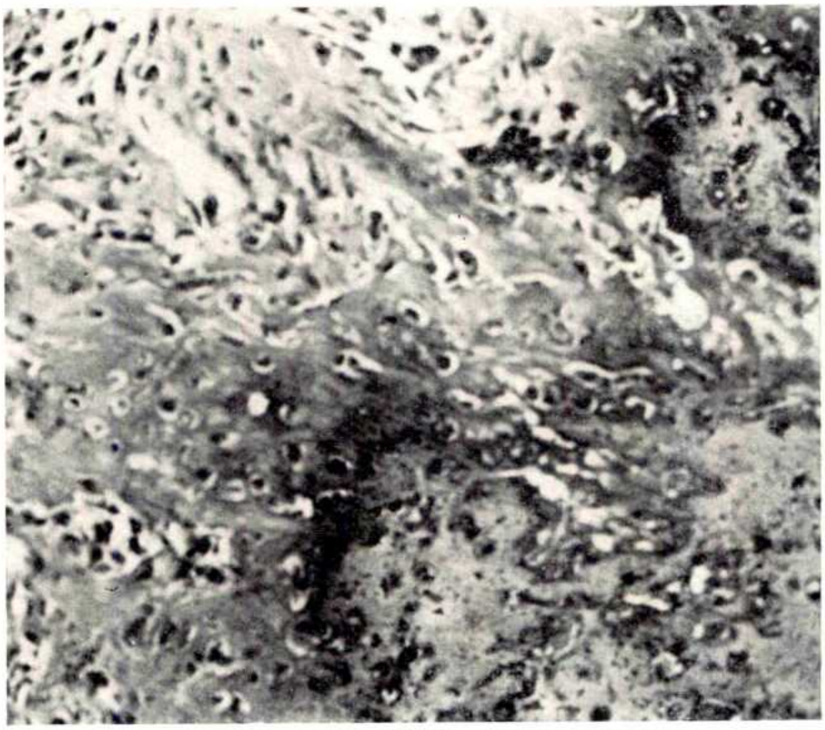

FIG. 4

Case 3, Formation of cartilage and bone. H. & E. × 140.

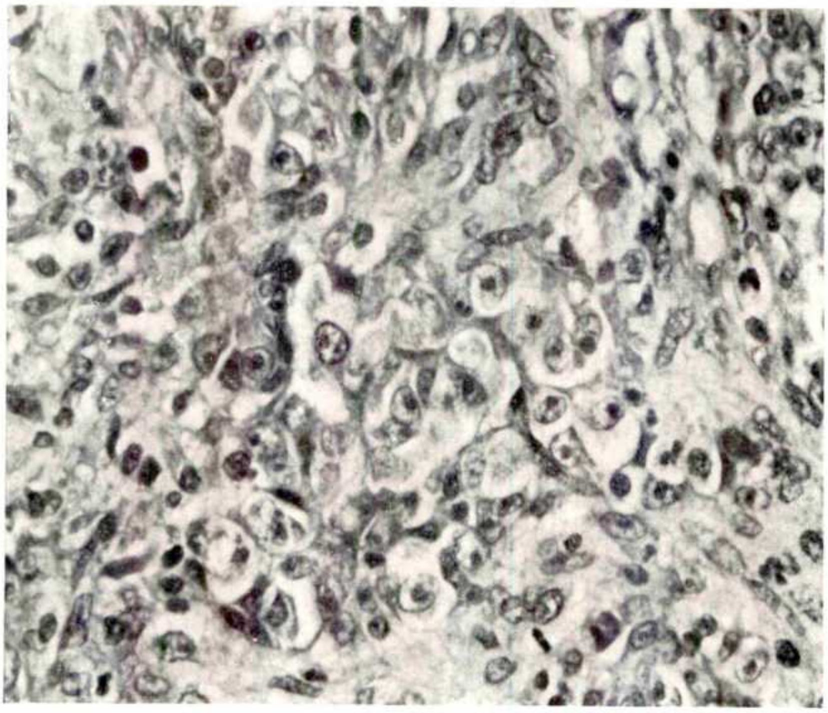

FIG. 5
Case 4, Carcinomatous areas. H. & E. × 350.

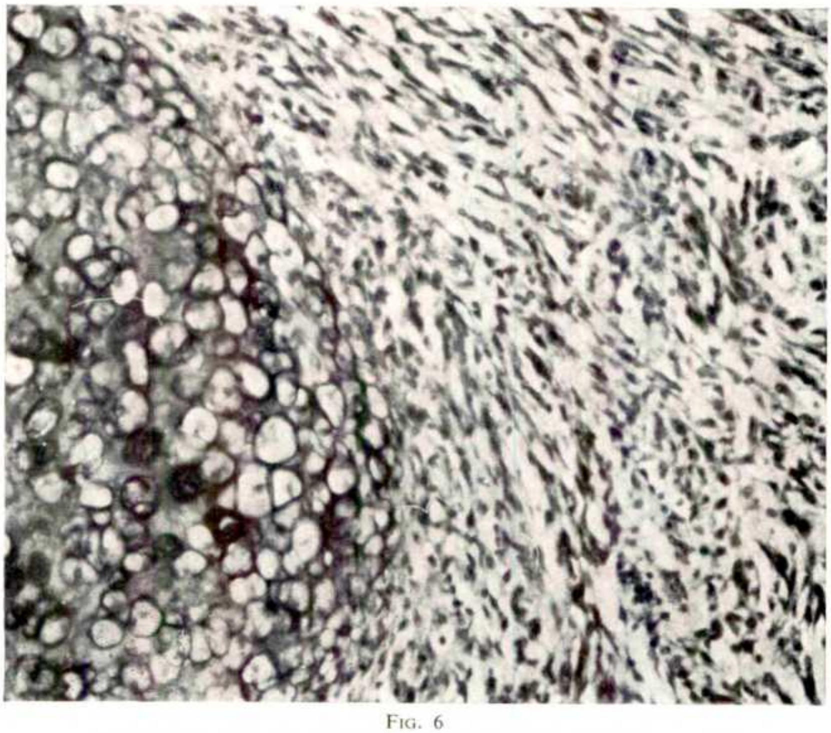

FIG. 6
Case 4, Sarcomatous areas with neoplastic cartilage. H. & E. × 140.

Case 3.—A man aged 65 was admitted to hospital complaining of intermittent hæmaturia of 1-week duration. Cystoscopy revealed a small tumour of the bladder wall and a transurethral resection was performed. Radiotherapy was given later and since then the patient has remained well for 3 years.

Three whitish fragments of tissue were examined. The appearances are those of a poorly differentiated carcinoma which in some areas shows a glandular formation (Fig. 3) while in others the tumour cells are producing mucin. The prostate was not clinically involved and there was no evidence of a gastro-intestinal carcinoma. The tumour was considered to be a primary adenocarcinoma of the bladder.

In some areas of the stroma, fibroblasts are enclosed within homogenous calcified material. Elsewhere there are areas of chondro and osteoplasia in all stages of evolution up to formation of mature cartilage or bone (Fig. 4). The mature bone has the shape of small plaques, within which there are tumour cells and capillaries.

Case 4.—A man aged 82 who underwent an operation for benign prostatic hyperplasia 5 years before the present admission. He was admitted to hospital with a history of hæmaturia of 2 weeks' duration.

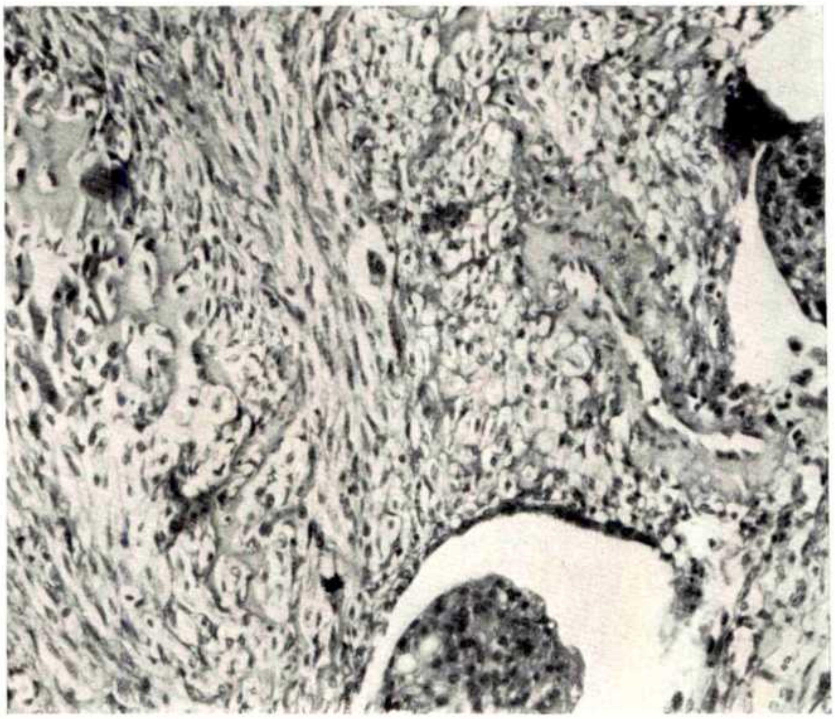

FIG. 7

Case 5, Mixed carcinomatous and sarcomatous tissue with bone trabeculæ. H. & E. × 140.

A cystogram showed a tumour but cystoscopy proved to be impossible. During the first days of his admission the patient passed small fragments of tissue with urine. Histological examination of these fragments suggested the presence of an undifferentiated carcinoma. At this stage a laparotomy was performed; the bladder was full of neoplastic tissue. As much as possible of the tumour was excised as a total cystectomy was considered impracticable. A few days after the operation the patient died. An autopsy was not performed.

In some areas the tumour has the appearance of an undifferentiated carcinoma (Fig. 5). The tumour cells have either a foamy, or deeply stained, cytoplasm, and are forming clumps within a stroma of connective tissue. Mucin is present within the cytoplasm of the foamy cells and mitotic figures are numerous. In other areas the neoplastic cells are spindle shaped with discrete boundaries and in some places with a network of fine collagen fibres, or they are more anaplastic and pleomorphic with numerous mitotic figures. Thus the appearances in these areas are those of a sarcoma.

Mucin is present in the cytoplasm of some of these cells and within the stroma between the fibres of collagen; giving a myxoid appearance. In other areas the neoplastic cells are forming primitive neoplastic cartilage which has focal areas of maturation (Fig. 6).

The appearances are those of two different tumours, a carcinoma and a sarcoma, but the two patterns merge so imperceptibly that there is no clear boundary between the two. This tumour, similar to those described in the urinary bladder by Frühling *et al.* (1959) can be considered as a "carcinosarcoma" according to the conceptions of these authors. The carcinomatous element of the tumour is an anaplastic carcinoma and the sarcomatous a fibro-myxochondrosarcoma.

Case 5.—A man aged 56 was admitted to the hospital complaining of hæmaturia. Cystoscopy revealed a small tumour of the bladder wall which was excised by transurethral resection. The patient remains well after 4 years.

Grossly the tumour had a papillary appearance. Histology showed two different growth patterns which are mixed in the deeper layers of the specimen.

The appearances are predominantly those of a moderately well differentiated papillary transitional cell carcinoma of the bladder. There is squamous metaplasia in some areas and a moderate number of mitotic figures.

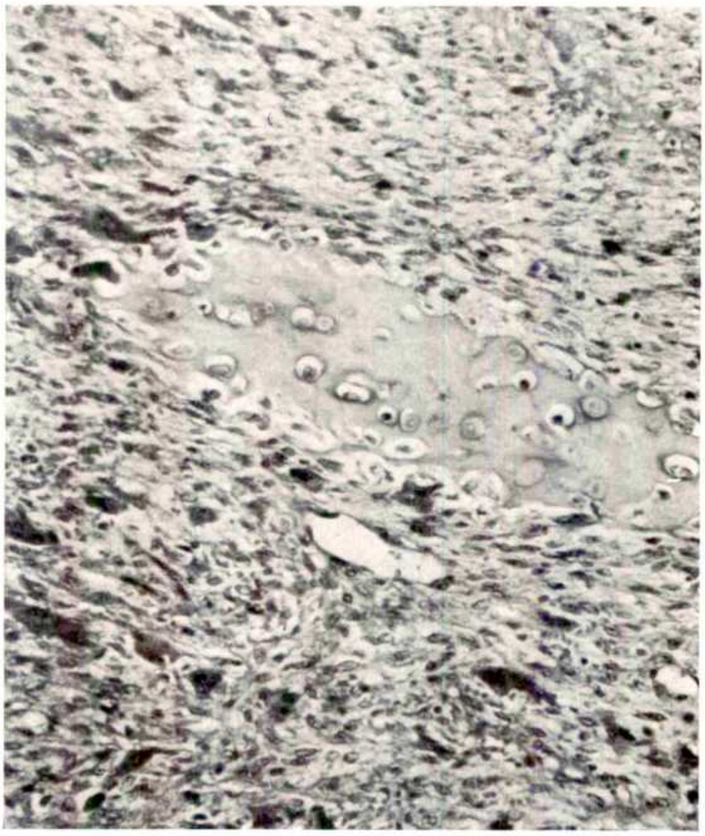

FIG. 8

Case 5. Sarcomatous tissue with neoplastic cartilage and osteoclasts.
H. & E. × 140.

The remainder of the tumour has the appearance of a sarcoma which, in several areas, is mixed with the carcinoma and forms the stroma of the clumps of malignant epithelial cells. In some areas of the sarcomatous element there is osteoid and in others there is mature calcified bone (Fig. 7). Osteoblasts as well as osteoclasts can be seen around the bone trabeculæ. In other areas cartilage is present (Fig. 8).

The tumour was considered to be a "carcinosarcoma of collision type" formed by the mixture of two different neoplastic elements, a transitional cell carcinoma and an osteo-chondrosarcoma.

DISCUSSION

Of the present cases 3 are carcinomas and the other 2 (cases 4 and 5) are carcinosarcomas. The present cases and those recorded in the literature can be divided into 3 main groups:

(*a*) Epithelial tumours (carcinomas) with bone or cartilage formation which is a result of metaplasia within their stroma.

(*b*) Mesenchymal tumours (sarcomas) in which bone or cartilage is a neoplastic element.

(*c*) Carcinosarcomas in which bone or cartilage formation is an element of their mesenchymal component.

The presence of bone within the stroma of carcinomas has been reported in the stomach, gallbladder, intestine, kidneys, uterus, breast, salivary glands, skin, prostate and lungs (Willis, 1962).

The first 2 published cases of carcinomas of the bladder with bone formation within their stroma were those presented by Pang (1958). Another case is recorded by Collins and Curran (1959) as an example of stromal ossification and the picture of a fourth appears in Armed Forces Institute of Pathology Atlas (Friedman and Ash, 1959). A fifth case was demonstrated by Theodossiou and Davillas at the Greek Society of Urology (1970). We have been unable to find any published record of an example of cartilaginous metaplasia in the stroma of a carcinoma of the bladder similar to the one observed in our third case (Table 1).

Bone may be formed in the stroma of bladder mucosa transplanted experimentally both in animals (Huggins, 1931; Constance, 1954; Galanos, 1963) and in man (Welcker, 1950). Although there was no cartilage formation observed in these experiments a cartilaginous metaplasia has been seen within the stroma of carcinomas of other organs (Willis, 1962).

It is surprising that only 7 cases of cartilaginous and bone metaplasia have been reported out of the many hundreds of carcinomas of the bladder which occur. A possible explanation for this is that in most cases malignant cells lose the bone- or cartilage-forming activity normally resident in bladder epithelium although no morphological difference between cells of carcinomas with and without osteoplasia has been observed. Alternatively this osteoblastic effect may be relatively ineffective on the non-neoplastic stroma of a carcinoma.

Deschamps, in 1791, described the first case of a bladder fibrosarcoma (cited by Deming, 1924), and up to 1956, 342 sarcomas of the bladder have been reported in the literature (Powers *et al.*, 1956). Among these, primary osteo-chondrosarcomas are very rare and to the present time only 14 cases have been reported (Table II).

The term " carcinosarcoma " was introduced by Virchow (1864) to describe a tumour which according to his opinion had 2 different histological malignant elements: epithelial and mesenchymal, with the same cellular origin. Meyer (1930) used the term " kombinations tumor " for this in contrast to the " Kompositionstumor " in which the causative factor of the neoplasia of the one component is the neoplasia of the other. Although the existence of those carcinosarcomas is denied by many authors (Tossios, 1964) the term is still used for the description of tumours formed of a secondary mixture of two different and separately growing malignant elements (" kollisiontumor ") (Meyer, 1930).

These carcinosarcomas are very rare in the urinary bladder but in those which do occur the presence of cartilage and bone is relatively common. Thus among the 30 reported cases of these tumours 13 contained either cartilage, bone, or both, as an element of their malignant mesenchymal component. In his monograph, " The Borderland of Embryology and Pathology ", Willis (1962) questions: " Is the comparative frequency of the combination of osteogenic or chondrogenic sarcoma and epithelial growth in the bladder related in any way to the peculiar bone-inducing capacity of urinary tract epithelium? " According to Pang (1958) " it seems clear that the bone-evoking power of the urinary epithelium is not due to its cell specificity but to its chemical and enzymatic products ". However, cartilage formation within the carcinosarcomas is much more common than bone formation. Of the 13 cases (Table III) all except 1 contain cartilage, 3 contain bone and cartilage, and 1 bone only.

In answer to the question whether there is any cartilage-evoking activity of the urinary epithelium, Willis (1962) suggests: " Perhaps the degraded epithelial mucin may conjugate with, or otherwise alter, the connective tissue mucins, and perhaps this material may sometimes

TABLE I

Carcinomas with Osseous and Cartilaginous Metaplasia of their Storma

Author	Year	Patient		Histology According to Author				Comments
					Stroma			
		Sex	Age	Tumour	Osteoid	Bone	Cartilage	
Pang . . .	1958	F	60	Trans. cell carcinoma	+	+	–	...
Pang . . .	1958	M	50	Papilloma with early carcinomatous change	+	+	–	...
Collins and Curran	1959	M	68	Villous tumour	+	+	–	A picture as example of stromal ossification
Friedman and Ash	1969	M	68	Carcinoma	+	+	–	A picture in armed Forc. Inst. Atlas
Theodossiou and Davillas . .	1970	M	60	Anaplastic carcinoma	+	+	–	...
Delides (case 1) .	...	M	65	Trans. cell carcinoma	+	–	–	...
Delides (case 2) .	...	M	56	Trans. cell carcinoma	+	+	–	...
Delides (case 3) .	...	M	65	Adenocarcinoma	+	+	+	...

TABLE II

Primary Osteo-chondrosarcomas of the Bladder

Author	Year	Patient		Histology			Term Used by Author	Comments
		Sex	Age	Osteoid	Bone	Cartilage		
Ordonez . . .	1856	M	old	–	–	+	Secondary chondroplasia	Cited by Shattock, debatable
Beneke . . .	1900	M	72	+	+	+	Osteoid chondrosarcoma	Cited by Pang
Heisler . . .	1905	...	...	–	–	+	Fibro-œdemato-myochondroma	Cited by Crane and Trembley
Fisher . . .	1908	F	62	+	+	+	Osteoid chondrosarcoma	...
Reid . . .	1913	M	67	+	+	+	Chondromyxosarcoma	...
Wright-Smith . .	1929	M	47	+	+	+	Malignant teratoma	...
Droschl . . .	1937	M	67	+	+	–	Osteoid sarcoma	...
Crane and Trembley .	1943	M	69	+	+	+	Osteogenic sarcoma	
Hirsch and Gassez .	1944	M	83	+	+	+	Cancerous mixed tumour	Description confirms with an osteo-chondrosarcoma
Jones and Ross .	1951	F	44	+	+	+	Osteogenic leiomyosarcoma	...
Nourse . . .	1957	M	44	+	+	+	Osteogenic sarcoma	...
Pang . . .	1958	M	74	+	–	–	Osteosarcoma	...
Nikolai and Spjut .	1959	F	66	+	+	+	Osteosarcoma	...
Kikuchi, Nakamura and Nakajima .	1965	M	47	+	+	–	Osteogenic sarcoma	...

approach chondromucins in composition and so induce the connective tissue to chondrify ". We demonstrated PAS positive epithelial mucin in cases 3 and 4 but not case 5.

Considering the frequency of the presence of cartilage and/or bone in carcinosarcomas of bladder it seems that a sarcoma of the organ tends to be a primary chondrosarcoma or, less commonly, an osteo-chondrosarcoma in the presence of malignant epithelial cells. This suggests that cells of the epithelial component of a carcinosarcoma do not lose their cartilage or bone-forming activity. It may also suggest that the malignant mesenchymal cells are more susceptible to the cartilage or bone evoking factors of the epithelial cells. This feature is probably related to the " embryonal " state of the sarcomatous stromal cells which more readily undergo metaplasia, with formation of cartilage and bone, than do the mature mesenchymal cells which form the stroma of a carcinoma.

TABLE III

Carcinosarcomas of the Urinary Bladder with Chondro and Osteoplasia

Author	Year	Patient		Histology as Described by Author				Term Used by Author
				Epithelium	Mesenchymal			
		Sex	Age		Osteoid	Bone	Cartilage	
Shattock . .	1887	M	55	Papilloma	–	–	+	Chondrifying sarcoma with multiple papillomata
Renner . .	1931	M	71	Trans. cell carcinoma	–	–	+	Fibro-myxochondro-carcinoma
Pollack . .	1936	M	72	Clubs of epith. cells	–	–	+	Malignant teratoma
Arnold . .	1941	F	43	Glandular and cornified carcinoma	–	–	+	Teratoid carcinosarcoma
Powers, Hawn and Carter . .	1956	M	79	Trans. cell carcinoma	+	+	+	Osteogenic sarcoma and Trans. cell carcinoma
Pang . . .	1958	M	74	Trans. and squamous cell carcinoma	–	–	+	Mixed tumour
Pang . . .	1958	M	74	Trans. cell carcinoma	+	+	+	Mixed tumour
Frühling, Batzen-schlager and Blum. . .	1959	M	71	Papillomatous carcinoma	–	–	+	"True" epitheliosarcoma
Frühling, Batzen-schlager and Blum. . .	1959	F	65	Undifferentiated carcinoma	–	–	+	"True" epitheliosarcoma
Frühling, Batzen-schlager and Blum. . .	1959	F	73	Undifferentiated carcinoma	–	–	+	"True" epitheliosarcoma
Mioduszewska and Stapor . .	1962	M	71	Papilloma	+	+	–	Ossifying sarcoma with papilloma
Delides (case 4)	...	M	82	Undiff. carcin.	–	–	+	Carcinosarcoma
Delides (case 5) .	...	M	56	Trans. cell carcinoma	+	+	+	Mixed carcinosarcoma

Such a hypothesis would explain the rarity of bone and cartilage formation in the majority of bladder tumours but the nature of the hypothetical cartilage or bone evoking factors is still a matter for further investigation.

SUMMARY

Five new cases of tumours of the urinary bladder which include bone and cartilage have been found in a survey of 968 cases of bladder tumours seen in the Department of Pathology, University of Athens. Three are carcinomas and the other 2 are carcinosarcomas. It is suggested that cartilage or bone evoking activity of the urothelium is present in carcinoma cells but malignant mesenchymal cells are more susceptible to this change.

I should like to thank Professor D. S. Eleftheriou (Athens) for his help and advice and Professor W. A. J. Crane for his encouragement. In addition I am grateful to Drs L. Henry, A. Kennedy and J. C. E. Underwood for their assistance in the preparation of this paper.

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FACTORS REDUCING THE RATE OF INFECTION AFTER TRANS-URETHRAL SURGERY

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THE incidence of urinary infection after urological operations has varied widely. Rates varying from 6 to 100 per cent have been reported (Gillespie *et al.*, 1960; Singh *et al.*, 1969), but in few reports have the factors involved been identified and seldom has the distinction been made between contaminants and pathogens. The use of a closed system of urinary drainage into a receptacle, containing antiseptic, will prevent infection in more than 90 per cent of patients (Gillespie *et al.*, 1964; Webb and Blandy, 1968), but there still remains a substantial risk that catheter-borne urinary infection will occur even after closed operations on the urinary tract. Studies reported here were undertaken to investigate the other factors which might be significant in the occurrence of post-operative urinary infections:

1. Whether the previously observed infection rate could be maintained in an ordinary general surgical ward.
2. Whether a method of continuous irrigation would reduce the need to change the catheter and hence the infection rate.
3. Relationship between the operation and the onset of infection.
4. The effect of the type of operation on the incidence of infection.

Methods.—All patients studied were male and all procedures performed were trans-urethral. Patients who came to hospital with a catheter in place or who had been found to have any organisms present in the urine before operation were excluded from the studies. At operation the skin was cleaned with 0·5 per cent chlorhexidine with 70 per cent alcohol and the urethra was filled with 0·25 per cent chlorhexidine in 1 per cent lignocaine gel. All instruments were boiled, autoclaved or sterilised by pasteurisation in a Francis water bath. Trans-urethral resections were performed using autoclaved distilled water and sterile glycine as an irrigant. After each operation a 22 Ch Foley catheter was introduced and was connected to a continuous drainage bag, with a non-return valve, containing 10 ml., 5 per cent chlorhexidine.

In patients where irrigation was used, sterile physiological saline was continuously instilled into the bladder through a 3-way Foley catheter. Immediately after resection, saline was run in at the rate of 1 litre in the 1st hour and thereafter the rate of flow was adjusted according to the amount of blood in the effluent.

Infection was considered to be present if there was any growth in the urine on culture after 24 hours, daily specimens being obtained from the latex tubing of the catheter with a sterile syringe and needle. Infection was diagnosed when the bacterial count was greater than 10^5 bacteria per $cm.^3$. If clots obstructed the outflow tubing, they were " milked ". If this did not dislodge them, the bladder was irrigated using aseptic precautions with an autoclaved Riches bladder syringe and sterile saline. If this did not clear the catheter, it was changed.

RESULTS

Closed Drainage in an Ordinary Surgical Ward.—In the first study, further investigations were undertaken to establish whether the rate of urinary infection achieved earlier (Webb and

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Blandy, 1968) could be maintained when the method of closed system drainage previously described was used in routine ward practice. Forty-two patients were investigated. All had trans-urethral procedures and 33 of these were trans-urethral resections of the prostate. All had closed drainage. Forty of the patients remained uninfected in the post-operative period. Of these, 31 were trans-urethral resections of the prostate. The overall infection rate for all trans-urethral procedures was 5 per cent and for T.U.R. of prostate 6·4 per cent. These results confirmed that the system was comparable in infection rate with that reported earlier.

Post-operative Bladder Irrigation.—It seemed likely that infection would occur in those cases where the closed drainage was " broken ". This usually resulted from obstruction of the catheter by clot or debris, requiring syringing or changing of the catheter. We set out to find out whether an effective system of irrigation could prevent such obstruction and so reduce the incidence of infection.

TABLE I

Comparison on Infection Rate in Irrigation Group and in Straight Drainage Group

	Irrigation	Straight Drainage	P
No. of patients	93	57	
Catheter Changed	15	12	>0·30
Percentage	15·5	21·2	
Developed Infection	7	5	>0·99
Percentage	7·5	8·7	

TABLE II

Comparison of Infection Rates Between Patients Who had a Catheter Change and Those Who did not

No. of patients	No. Who Became Infected	Percentage	P
Catheter changed 27	5	18·5	>0·01
No. catheter changed 123	7	5·7	

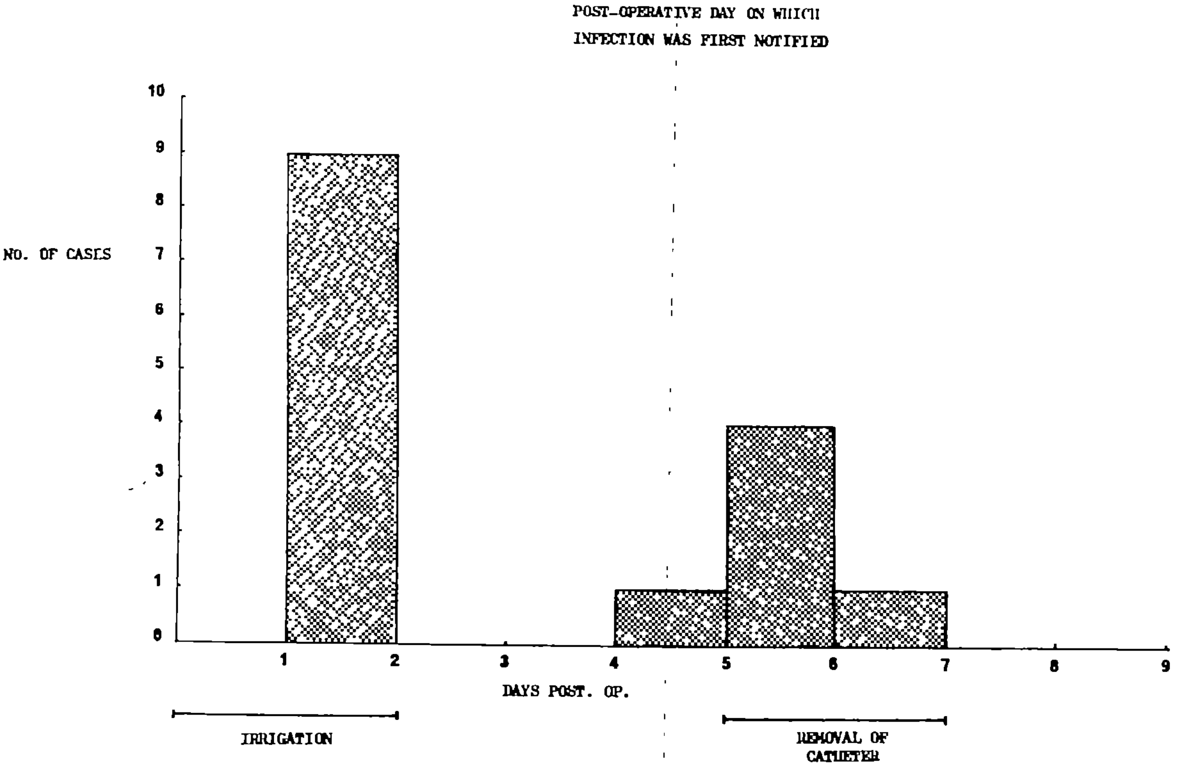
One hundred and fifty patients were studied. The catheter was managed in either of two different ways after operation:

Group A (*Straight Drainage*).—In 57 patients the catheter was connected directly to a plastic bag containing chlorhexidine, as already described. Five out of 57 patients became infected (8·7 per cent). Twelve had to have their catheter changed (21 per cent) and 2 of them became infected.

Group B (*Continuous Saline Irrigation*).—In 93 patients, a 3-way Foley catheter was inserted and a continuous irrigation of the bladder with sterile physiological saline was carried out, the drainage being through a similar closed system. Seven out of 93 patients developed infection (7·5 per cent), 15 had to have their catheter changed (16 per cent) and 3 of these became infected (Table I).

Although irrigation reduced the need to break the closed system to wash out the bladder, there was a negligible reduction in the infection rate. This was surprising, since a change of catheter (27 in 150 patients, *i.e.* 18 per cent) was associated with an increased rate of infection (Table II).

Delay Between Operation and the Onset of Infection.—This failure of continuous irrigation to reduce the post-operative rate of infection led us to pay closer attention to the interval between the operation and the onset of infection. A further series of 100 patients was studied. All had continuous irrigation following trans-urethral resection of the prostate. This was discontinued when clots had stopped forming, and the catheter was removed when obvious fresh hæmaturia had cleared.



Figure

Fifteen of these patients had infection with bacterial counts of greater than 10^5 organisms per $cm.^3$ at some time within the post-operative period. Nine of them developed infection in the second post-operative 24 hours, *i.e.* during the period of irrigation, but in only 1 of them did the infection persist after the patient was discharged from hospital. In 5 patients, infection was noted only after the catheter was removed, but in 3 of these it persisted after discharge from hospital (Figure 1). One of the patients became infected after the irrigation had been stopped and before removal of the catheter.

Three months later, only 4 of the patients were still infected and all had unrelieved urological conditions. One had a carcinoma of the prostate, one had persistent hæmaturia from chronic cystitis and the other two had developed urethral strictures.

Type of Operation and the Incidence of Infection.—In 42 of the patients studied in section 3, we considered the relationship between infection and type of operation. Seven of these patients had become infected in the post-operative period.

(a) *Weight of Prostate Resected.*—The wet prostatic chippings were weighed to the nearest gram. In the 35 non-infected patients the mean value was 9 g. In the patients who became infected (7 patients) the mean value was 19 g.

(b) *Duration of Resection.*—This was measured from the time of the first cut with the resectoscope to the insertion of the catheter. In the non-infected group the mean time was 19·6 and in the infected group, 30·2 minutes.

(c) *Duration of Post-operative Catheter Drainage.*—In the non-infected group the mean duration of catheter drainage was 73 hours and in the infected group 105 hours.

(d) *Blood Loss at Operation and in the Immediate Post-operative period.*—The bladder washings at operation were collected in a measured water bath and the blood loss was estimated colorimetrically by the acid hæmatin method (Sahli, 1931). In the post-operative period all bladder washings were collected and each 10-litre sample was estimated until macroscopic hæmaturia had ceased. The accuracy of this method was found to be + or − 5 per cent by the use of test samples (Nesbit and Conger, 1941). The blood loss in the non-infected group was approximately half that of the infected group. In neither group was it excessive; the mean loss during operation being 95 c.c. in the non-infected group and 160 c.c. in the infected group, to which must be added post-operative losses of 171 c.c. and 358 c.c. respectively (Table III).

TABLE III

		Infected	Non-infected	Significance
Resection time	Mean	30·2 min.	19·6 min.	P>0·05
Blood Loss				
1. During	Mean	160 c.c.	95 c.c.	P>0·2
2. Post-op.	Mean	358 c.c.	171 c.c.	P>0·1
3. Total	Mean	532 c.c.	263 c.c.	P>0·05
Weight of prostate	Mean	19 g.	9 g.	P>0·01
Catheter time	Mean	108 hr.	73 hr.	P>0·005

DISCUSSION

Although closed drainage into a plastic bag containing antiseptic was found to be easy to manage and the infection rate, even during prolonged routine ward use, remained about 6 per cent, we felt that this was still too high to be regarded with any degree of complacency. We were disappointed to see that the use of post-operative continuous saline irrigation did not improve this infection rate, even though we were able to reduce the need to break the aseptic closed system in order to remove clots or irrigate the catheter.

We expected that reducing the formation of clots and catheter blockage by continuous irrigation should reduce the incidence of infection. On the contrary, our results suggested that irrigation increased the incidence of infection. True, the majority of these infections did not cause any clinical symptoms, or persist after discharge from the hospital, nevertheless, some of them did and not one can be accepted without concern. It may be that irrigation should be discontinued on this account or that other methods of " irrigation " may be better, *e.g.* self-irrigation by means of diuretics (Essenhigh, 1969).

Our experience shows that patients who have small resections, short resection time, and minimal blood loss have a small risk of becoming infected. The longer the catheter was needed, the greater the incidence of infection. If patients had their catheter removed in under 72 hours, they had a much better chance of escaping post-operative infection. The fact that the infections associated with prolonged catheter drainage could sometimes persist long after discharge from hospital, suggests that this type of infection, unlike that associated with irrigation should be taken seriously.

Although we have not yet made a formal study of the reasons which lead to prolonged catheter drainage, it seems likely that there are two main factors: delay in the return of bladder tone, and the persistence of bleeding. It is therefore essential to stop the bleeding at operation and it may be useful to study the performance of the detrusor by cystometrography before operation.

We seem here to have reached the situation, which is common in other surgical fields, where the elimination of gross sources of sepsis leads to a gratifying reduction of the infection rate but not a complete prevention of it. We seem to be now facing the hard core of the problem, the 5-8 per cent of patients who become infected in spite of all our best endeavours. None of these groups of patients had " prophylactic " antibiotics at any time. Perhaps the right antibiotic given at the right instant to the right case could still further reduce this hard core. Five per cent infection rate may be considered reasonable when measured against contemporary statistics, but urological surgery needs to be as aseptic as orthopædic surgery, ophthalmology or neurosurgery, and 5 per cent is too high an infection rate for complacency.

SUMMARY

A series of investigations were undertaken to study urinary infections following trans-urethral surgery. These showed that closed catheter drainage achieved an infection rate of 5 per cent. Continuous saline irrigation did not reduce this rate and may even increase it, as did prolonged catheter drainage. Patients with small resections, short resection times and minimal blood loss had a smaller risk of becoming infected. Infections associated with prolonged catheter drainage, unlike those associated with irrigation, tended to persist even after discharge from hospital.

We are grateful for the help in carrying out these studies which we have received from Mr D. Jarvis and the staff of the Department of Microbiology and from the nursing and secretarial staff of the London Hospital.

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THE URINARY PARTICLE SCAN: A TRACER TECHNIQUE FOR DETERMINATION OF BLADDER BACTERIAL RESIDUAL[1]

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The normal urinary bladder is able to resist infection despite repeated contamination by viable bacteria. Two mechanisms seem to be responsible: the inherent resistance factors of the bladder wall and urine medium (Norden *et al.*, 1968) and the actual reduction in the number of bacteria by the mechanical act of voiding. The efficiency of the second mechanism depends on the frequency of voiding and the completeness of emptying following a single void. Studies to date have only involved indirect measurements, calculating the remaining bacteria after voiding by subtracting the number of organisms eliminated from a known inoculum, and have assumed uniform suspension of the bacteria in the urine (Cox and Hinman, 1961).

Previous investigations in our laboratory have shown that radioactive sulphur colloid particles behave like bacteria when introduced into the urinary tract (Corriere *et al.*, 1968, 1969) and that their movement can be studied with external radionuclide scanning. We have now used this technique to directly evaluate the effectiveness of repetitive, equal-interval voiding in reducing bacterial contamination of the human bladder and propose its use as an adjuvant diagnostic aid for the patient with recurring urinary tract infections.

Materials and Methods.—Sulphur colloid particles were prepared and tagged with 99 m. technetium, a gamma-emitting isotope, according to the modified method of Larson and Nelp (1966). These particles are approximately bacterial size (2-5 microns) and remain stable over a pH range of 2-8. Efficiency of tagging and uniformity of particle size was confirmed with microscopic inspection using a standard red cell chamber and Packard chromatogram scanner.

Fifteen patients were initially classified into three groups according to their clinical history and routine diagnostic procedures (urine analysis and culture, excretory urogram, voiding cysto-urethrogram and cystoscopy). These groups, as seen in Table I, were (1) *definitely normal*: patients with sterile urine, no significant residual urine after voiding and no symptoms of vesical dysfunction; (2) *definitely abnormal*: patients with large residual urine on the urogram, cysto-urethrogram and in the post-catheterisation specimen, symptoms of bladder dysfunction and infected urine; (3) " *uncertain* " *clinical diagnosis*: patients with symptoms of recurring cystitis with frequently positive urine cultures but without other positive diagnostic findings. All of these patients emptied their bladders completely of urine with a single void. They were all asymptomatic and uninfected at the time of study.

The radioactive particles (0·5 to 1·0 mCi) were introduced in a sterile manner into the urinary bladders of the patients with a urethral catheter and followed with 100-150 c.c. of sterile saline. The patients were well hydrated before the study and not restricted or medicated in any way. They were then scanned on a modified dual probe rectilinear scanner, and the data recorded on perforated paper tape. Radionuclide distribution (Fig. 1) was quantified by a processor (Kuhl and Edwards, 1969) that displayed the data as either a scan image from a cathode ray

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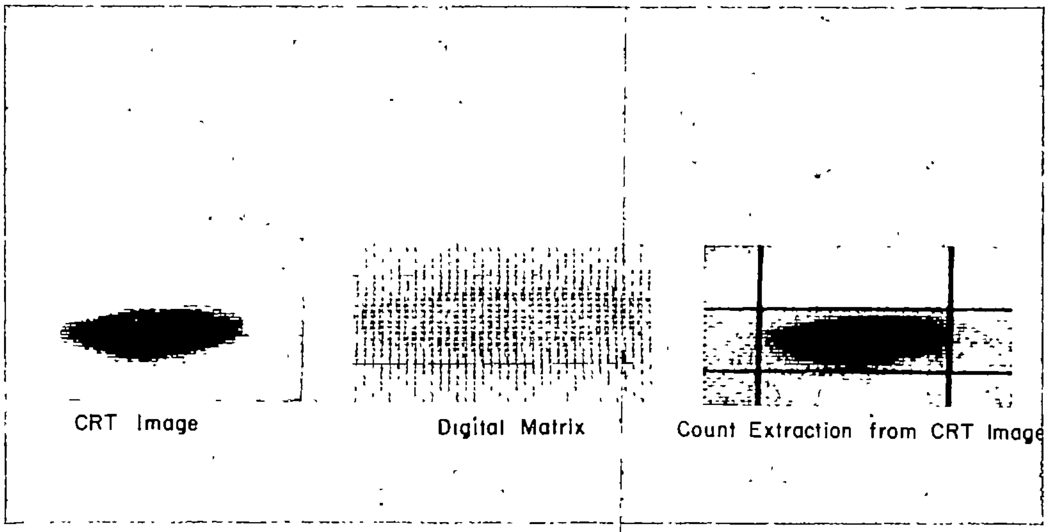
TABLE I

Patient	Age/Sex	Clinical History	Diagnostic Findings
		I. Definitely normal bladder function	
J. C.	42/F	Left renal mass	Renal mass on I.V.P.
E. S.	18/M	Proteinuria	Proteinuria
		II. Definitely abnormal bladder function	
F. B.	5/M	Recurrent fever and enuresis	Large residual urine, bilateral hydroureters and hydronephrosis
L. G.	26/M	Feeling of " inability to void "	Neurogenic bladder, 200 c.c. residual urine
		III. " Uncertain " clinical diagnosis (recurrent cystitis, neg. studies)	
M. B.	20/F	Bladder " discomfort "	Occasionally infected urine
A. S.	27/F	Recurrent urinary tract infections	Ocasionally infected urine
N. H.	25/F	Recurrent hæmorrhagic cystitis	Occasionally infected urine
J. R.	4/F	Recurrent urinary tract infections, enuresis	Occasionally infected urine
S. G.	72/M	Recurrent urinary tract infections after TURP	Repeatedly infected urine
B. M.	30/F	Recurrent urinary tract infections, low back pain	Occasionally infected urine
C. H	22/F	Recurrent urinary tract infections, low back pain	Occasionally infected urine
C. J.	25/F	Recurrent urinary tract infections	Occasionally infected urine
J. S.	28/F	Recurrent urinary tract infections	Occasionally infected urine
M. E.	32/F	Recurrent urinary tract infections	Occasionally infected urine
A. L.	4/F	Recurrent urinary tract infections, enuresis	Occasionally infected urine


CRT Image

Digital Matrix

Count Extraction from CRT Image

FIG. 1

Radionuclide displays of the human bladder: Three forms of representation (CRT = cathode ray tube).

TABLE II

Patient	Clin. Class.	% Act. Remain*. $T_2 = \infty$	Theoret. % Activ. Increase			
			$T_2 = 20'$	$T_2 = 30'$	$T_2 = 40'$	$T_2 = 60'$
1. F. B.	Abnormal	V–0: 1·000	—	—	—	—
		V–1: 0·200	0·56	0·40	0·33	0·282
		V–2: 0·110	0·90	0·45	0·32	0·224
		V–3: 0·100	2·25	0·79	0·47	0·278
2. L. G.	Abnormal	V–0: 1·000				
		V–1: 0·150	0·42	0·30	0·25	0·211
		V–2: 0·090	0·72	0·36	0·25	0·178
3. M. B.	Uncertain	V–0: 1·000				
		V–1: 0·060	0·17	0·12	0·10	0·084
		V–2: 0·040	0·32	0·16	0·11	0·080
4. A. S.	Uncertain	V–0: 1·000				
		V–1: 0·045	0·13	0·09	0·075	0·063
		V–2: 0·028	0·22	0·11	0·078	0·055
		V–3: 0·009	0·42	0·15	0·088	0·052
5. N. H.	Uncertain	V–0: 1·000				
		V–1: 0·049	0·14	0·10	0·082	0·069
		V–2: 0·023	0·18	0·09	0·065	0·046
		V–3: 0·015	0·34	0·12	0·070	0·042
6. J. R.	Uncertain	V–0: 1·000				
		V–1: 0·050	0·141	0·10	0·084	0·07
		V–2: 0·016	0·128	0·06	0·045	0·03
7. S. G.	Uncertain	V–0: 1·000				
		V–1: 0·020	0·06	0·040	0·033	0·028
		V–2: 0·009	0·07	0·036	0·025	0·017
8. B. M.	Uncertain	V–0: 1·000				
		V–1: 0·040	0·113	0·080	0·067	0·056
		V–2: 0·009	0·070	0·035	0·024	0·017
		V–3. 0·003	0·065	0·023	0·013	0·018
9. C. H.	Uncertain	V–0: 1·000				
		V–1: 0·017	0·084	0·034	0·028	0·024
		V–2: 0·009	0·072	0·036	0·025	0·018
		V–3: 0·003	0·067	0·023	0·014	0·008
10. C. J.	Uncertain	V–0: 1·000				
		V–1: 0·006	0·017	0·012	0·010	0·008
		V–2: <0·001	—	—	—	—
11. J. S.	Uncertain	V–0: 1·000				
		V–1: 0·0095	0·027	0·019	0·016	0·013
		V–2: 0·0045	0·035	0·018	0·013	0·009
12. M. E.	Uncertain	V–0: 1·000				
		V–1: 0·0277	0·078	0·055	0·046	0·039
		V–2: 0·0060	0·048	0·024	0·017	0·012
		V–3: 0·0024	0·055	0·019	0·010	0·007
13. A. L.	Uncertain	V–0: 1·000				
		V–1: 0·052	0·147	0·104	0·087	0·073
		V–2: 0·034	0·270	0·135	0·095	0·067
		V–3: 0·0095	0·217	0·076	0·044	0·027
		V–4: 0·0062	0·400	0·093	0·049	0·024
14. E. S.	Normal	V–0: 1·000				
		V–1: 0·008	0·022	0·016	0·013	0·011
		V–2: <0·001	—	—	—	—
15. J. C.	Normal	V–0: 1·000				
		V–1: 0·008	0·022	0·016	0·013	0·011
		V–2: 0·002	0·016	0·008	0·005	0·004

* V–0 = Initial activity in bladder (100 per cent).
V–1 = Percentage activity in bladder after first voiding.
V–2 = Percentage activity in bladder after second voiding.
V–3 = Percentage activity in bladder after third voiding.
V–4 = Percentage activity in bladder after fourth voiding.

tube (CRT), a matrix of numbers representing detected counts within a unit area, or a CRT image with superimposed extraction window, enabling instantaneous summation of bladder activity.

In each patient an entire scan frame was obtained with the bladder full. The catheter was then removed, the patient voided, and another scan performed. Subsequently, rectilinear scans were obtained after repeated voidings at 30-minute intervals for 1 and 1½ hours or until the isotope had been reduced to background values.

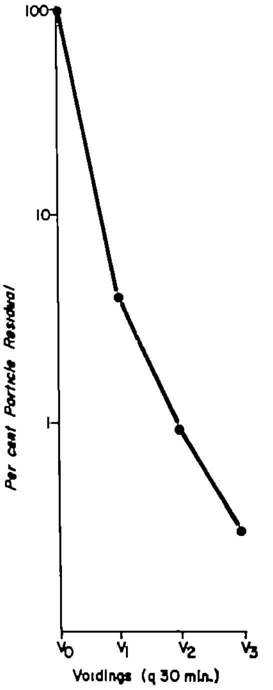


FIG. 2

Characteristic particle clearance pattern from representative patient (B. M.).

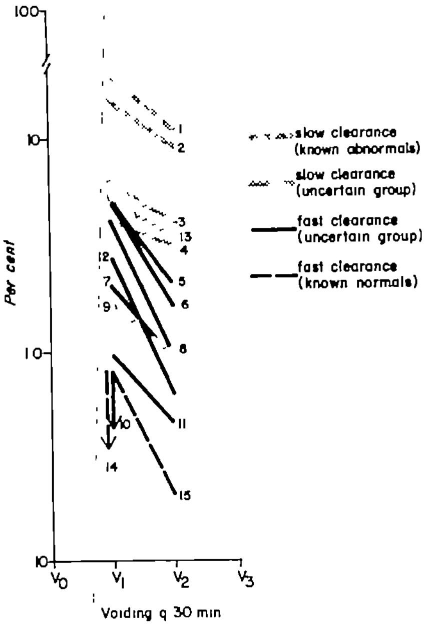


FIG. 3

Percentage of total bladder activity remaining in bacteriostatic system after voiding, as described by second component of particle clearance curves only (V_1-V_2). Vertical slope (10, 13) indicates residual at V_2 less than 0·001.

Results.—Four scans were obtained on each patient when possible. Digital data of isotope distribution in each scan frame was then displayed, the area summed and the retained activity calculated as the percentage of particles remaining after each void (Table II). This information was then graphically recorded on semilog paper as percentage residual activity *vs.* frequency of interval voiding. A characteristic particle clearance pattern (patient B. M.) is presented in Figure 2.

Most patients, except those with obvious bladder dysfunction, were able to void to a relatively small particle residual after the initial void. It appeared, however, that the second component of this clearance curve, *i.e.* the segment between the first and second voidings (V_1–V_2) best determined the overall efficiency of micturition (Fig. 3). As can be seen, the patient population seemed to separate into two sub-groups: one sub-group consisted of those patients having a slow particle clearance—a gradual slope to this second component of their clearance pattern; this group included those patients known to have abnormal bladder function (patients 1 and 2). The second sub-group consisted of those patients having a more rapid particle clearance—a steeper slope to this second component; this group included those patients known to be clinically normal (patients 14 and 15).

The data represented in this way, however, reflects a bacteriostatic system ($T_2 = \infty$). Since bacteria increase logarithmically at specific doubling rates (T_2), the data from each patient was mathematically corrected for doubling times of 20, 30, 40 and 60 minutes (Table II). In this way we can determine if a patient's efficiency of voiding is able to overcome the increasing number of proliferating bacteria present without adding the variable factors of bacterial death, local resistance and all of the other variables inherent in measurements of a biologic system. The data for a growth rate of $T_2 = 30$ minutes is presented in Figure 4; this is the approximate doubling rate of *Eschericia coli*, the most common urinary tract pathogen (O'Grady and Cottell, 1966).

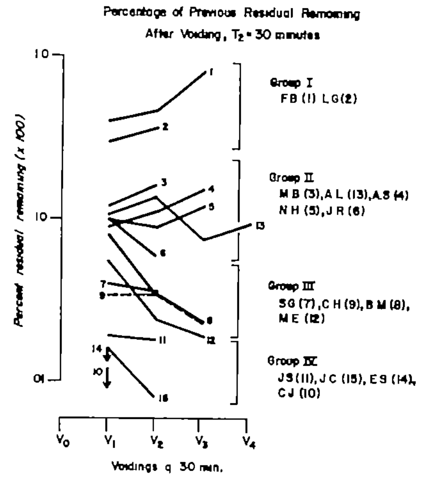


FIG. 4

Percentage of total bladder activity remaining after voiding under the condition of a theoretical particle (bacterial) doubling time of 30 minutes. Vertical slope (10, 13) indicates residual at V_2 less than 0·001.

Inspection of this graphical data shows a wider patient spread than in the bacteriostatic system, allowing classificating of the patients into four groups. The patients in Group I have the poorest clearance patterns and were those patients with known clinical abnormalities. Those in Group IV have the most rapid and efficient particle clearance patterns; this group includes those patients (14 and 15) known to be clinically normal as well as two patients whose clinical status was originally " uncertain ". Groups II and III contain a spectrum of clearance patterns from patients that seemed clinically homogenous. Those in Group II demonstrated difficulty in particle elimination, describing a system in which bacterial growth exceeds voiding efficiency. Group III, however, is composed of patients from the same clinical category as in Group II, but demonstrate a rapid clearance of particles, thereby describing a system in which voiding efficiency exceeds bacterial growth potential.

Patients showed little variation in classification as T_2 increased or decreased. It would seem, therefore, that the rate of bacterial growth, within physiologic limits, does not significantly influence a patient's ability to clear a bladder infection by voiding alone.

DISCUSSION

Establishment of a bladder infection following a bacterial inoculation depends on whether the increase in bacterial population exceeds the decrease caused by voiding and/or any intrinsic antibacterial action of the bladder wall and urine medium.

Many investigators have studied these two host defence mechanisms, but previous techniques used to evaluate the efficiency of micturition by analysing fluid residual or eliminated bacteria have involved indirect methods of quantification, the assumption that fluid and particles are eliminated at the same rate and significant technical difficulty (Lindbjerg and Brandt, 1964). Our study has shown that these assumptions are invalid.

The efficiency of voiding has also been studied from an essentially mathematical viewpoint (Boen and Sylwester, 1965; Hinman and Cox, 1966). The same basic assumptions noted above are also necessary, however, in a study of this type; and, as our work has demonstrated, the concepts thus employed, *e.g.* a " constant percentage residual " or " constant volume residual " have not proven physiologically sound. Consequently, these purely mathematical models remain primarily academic and without true clinical relevance.

We have previously shown in both the experimental animal and man (Corriere *et al.*, 1970) that fluid and particles are not handled identically by the upper urinary tract. When fluid refluxes into the undilated renal pelvis, as seen in the standard cinefluorographic study, it quickly returns to the bladder in less than 30 minutes, as does the fluid component of urine. Refluxed 99 mTc sulphur colloid particles placed in the bladder of an animal that freely refluxes or in the human with vesico-ureteral reflux, however, have been found to stay in the upper urinary tract for several hours. Because of this disparity between hydrokinetics and particle dynamics in the upper urinary tract, we have approached the problem of vesical bacteriuria by studying the clearance of bacteria-like colloid particles from the human bladder rather than monitoring fluid residual alone. By evaluating the ability of the bladder to void this colloid suspension correlated with the added factor of bacterial proliferation, comparison to the clearance of an activity growing bacterial inoculum can be directly made.

While many patients with urinary tract infections can be diagnosed using coventional techniques, a large group remains whose clinical status and efficiency of micturition are uncertain. While the majority of patients studied here appeared at first to be clinically homogeneous, a spectrum of function was found when each was studied in terms of his ability to void a bacteria-like inoculum. Routine diagnostic procedures had, therefore, missed a functional difference in this investigative group.

The pathophysiology responsible for prolonged particle clearance in these patients remains obscure. One could envisage a mucosal abnormality resulting from recurrent infection with its subsequent fibrotic changes. This is, in part, supported by the recent work of Weber *et al.* (1969) showing increased regional 131-MAA collections in the lumen of blood vessels containing fibrin deposition secondary to intimal injury. On the other hand, a neurologically dysfunctional bladder with an abnormal voiding profile could develop increased mucosal folds and diverticula which would afford areas for particle trapping. Any of these phenomena could prolong the clearance rate of particulate material from the bladder without disturbing fluid elimination and could, in part, account for the disparity between fluid and particle dynamics in the diseased urinary tract.

SUMMARY

Previous techniques used to evalute the efficiency of elimination of bacteria during voiding have involved the indirect measurement of the eliminated bacteria or determinations of fluid residual. We have developed a new technique for directly evaluating this voiding efficiency using external radionuclide scanning of bacteria-like 99 m. technetium sulphur colloid particles. We have studied the bladder clearance of these particles in 15 patients mimicking bacteriostatic conditions, and have mathematically corrected the data to simulate various bacterial growth rates. Routine diagnostic procedures failed to show bladder dysfunction in 11 subjects evaluated with recurring urinary tract infections, however, our study was able to define difficulties in particle (and presumably bacteria) elimination in 5 of these patients.

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SOLITARY TESTICULAR METASTASIS FROM CARCINOMA OF THE PROSTATE

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SECONDARY tumours of the testis are unusual pathological findings and rarely present as a clinical problem. They may metastasise from number of primary sites including the reticulo-endothelial system, lung, bowel, and prostate (Bradham, 1951; Arduino, 1955). Of 1,600 testicular tumours reviewed from the Armed Forces Institute of Pathology, there were 38 secondary cases, of which 12 were prostatic in origin (Price and Mostofi, 1957).

Prostatic carcinoma can spread to nearly any tissue in the body, but metastases to certain areas are rare. A single case of testicular dissemination was first reported in 1938 and a critical review of the literature reveals 37 additional cases (Herbut, 1952; Kay, *et al.*, 1954; Howard, *et al.*, 1957; Ichikawa, *et al.*, 1962). Bilateral testicular involvement was present in 10 of these and widespread metastases in all but 5 patients (Ney, *et al.*, 1959; Malek and Madsen, 1969; Marble, 1960; Markland, 1968).

The diagnosis of adenocarcinoma of the prostate with metastasis to the testis was suspected clinically in only 6 instances (Price and Mostofi, 1957). The remainder were discovered after therapeutic orchiectomy or at autopsy. Interestingly enough, in 2 cases the testicular abnormality was the first indication of the disease thus imitating a primary tumour (Price and Mostofi, 1957). To the best of our knowledge there has been no case report of simultaneous prostatic and primary testicular tumours.

CASE REPORTS

The first case is most unusual in that the secondary lesion was suspected pre-operatively and there was no evidence of other metastatic foci. Also, the 10-year lapse between the initial diagnosis of the primary tumour and the subsequent secondary manifestation is the longest recorded in literature.

Case 1.—F. P. S. 004-05-37-26.—A 75-year-old Caucasian male presented with a hard, 2×2 cm. mass on the lateral aspect of the lower pole of the left testis.

The patient was originally seen 10 years previously when he was admitted with azotemia and acidosis following a history of progressive obstructive urinary symptoms. He was found to have outlet obstruction secondary to adenocarcinoma of the prostate. There was no evidence of metastatic spread. Following trans-urethral resection of the prostate, the patient was placed on stilbœstrol, 5 mg. daily, and finally discharged in good condition. Seven years later he presented again with obstructive symptoms and hæmaturia. Once more there was no evidence of metastasis and he underwent trans-urethral resection of 22 g. of prostatic carcinoma. Practically all of the prostatic chips submitted contained adenocarcinoma of the prostate of varying degree of differentiation. Perineural invasion was present. He was maintained on 1 mg. of stilbœstrol daily.

Follow-up examinations over the next 3 years were unremarkable until he was seen 10 years after his original surgery. The patient was not aware of the testicular lesion. His weight and strength were stable and he was pain-free. Aside from occasional nocturia, he had no urinary symptoms. Physical examination disclosed no adenopathy. The breasts were enlarged but not tender. There was no back tenderness. The testes were atrophic but a 2 cm. hard, painless mass was present in the lower pole of the left testicle. Digital rectal examination of his prostate revealed irregular firmness on the left with possible extension near the base. The hæmogram was unremarkable, and a urine culture showed no growth. Serology was non-reactive and the blood urea nitrogen, creatinine, alkaline and acid phosphatase determinations were within normal limits. A urine gravindex test for chorionic gonadotrophins was negative. The chest film and bone survey were negative for metastasis.

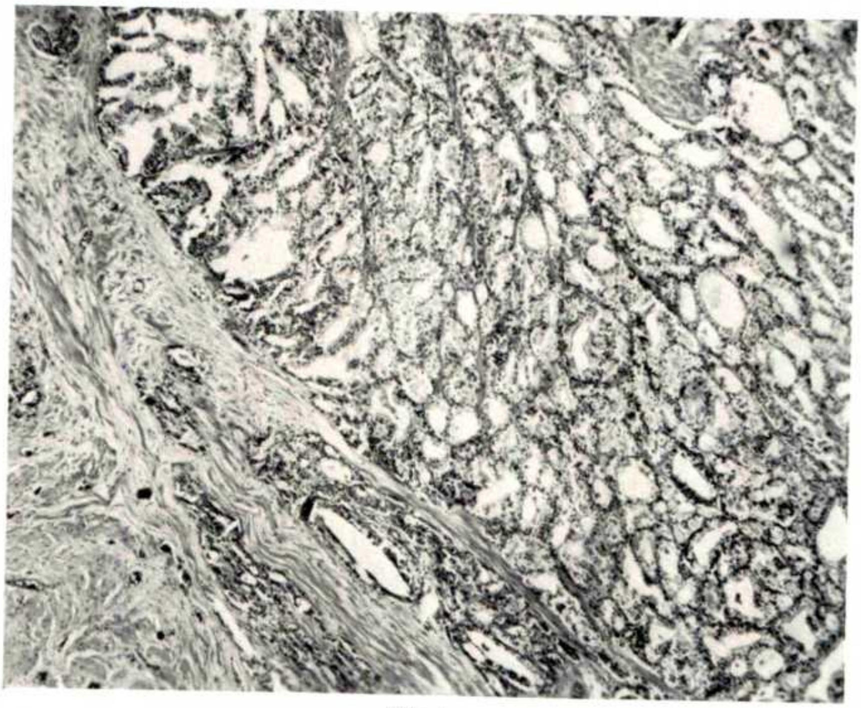

FIG. 1

Adenocarcinoma of prostate in resected specimen. There was perineural invasion in other areas (not shown here). × 50.

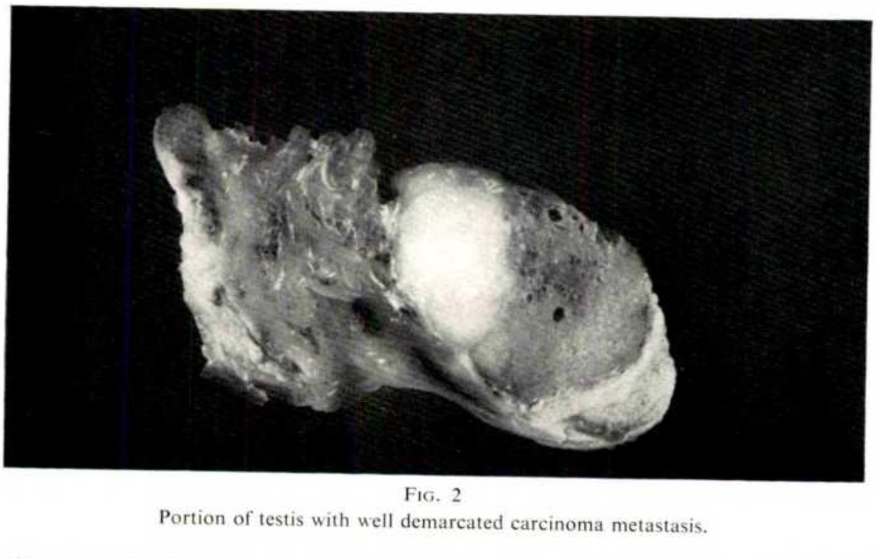

FIG. 2

Portion of testis with well demarcated carcinoma metastasis.

Exploration of the left testicle was accomplished through a left inguinal incision. A hard irregular mass was palpable beneath an intact tunica albuginea. The spermatic cord and epididymis were free of tumour. A left radical orchiectomy was performed. The patient's post-operative course was benign.

Pathology.—The resected testicle measured 3 × 2 × 3 cm. (Fig. 2). The parenchyma was tan-brown and atrophic. A firm, pale-yellow, sharply demarcated, nodular mass (which measured 2 × 1, 8 × 1·5 cm.) was situated at its lower pole.

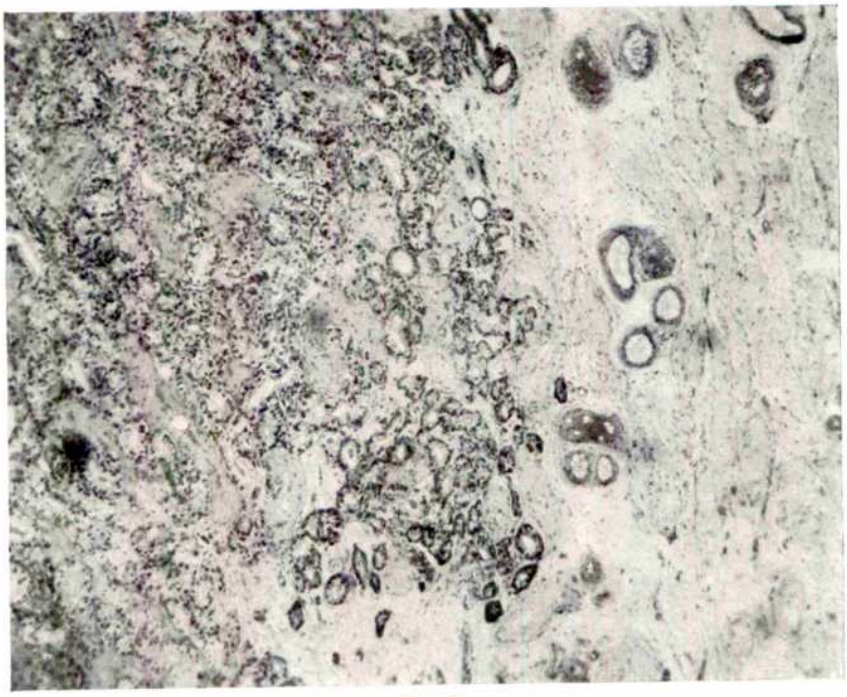

FIG. 3

Microscopic appearance of carcinoma metastasis to testis. Atrophic, hyalinised seminiferous tubules recognisable in lower portion of picture. (× 50.)

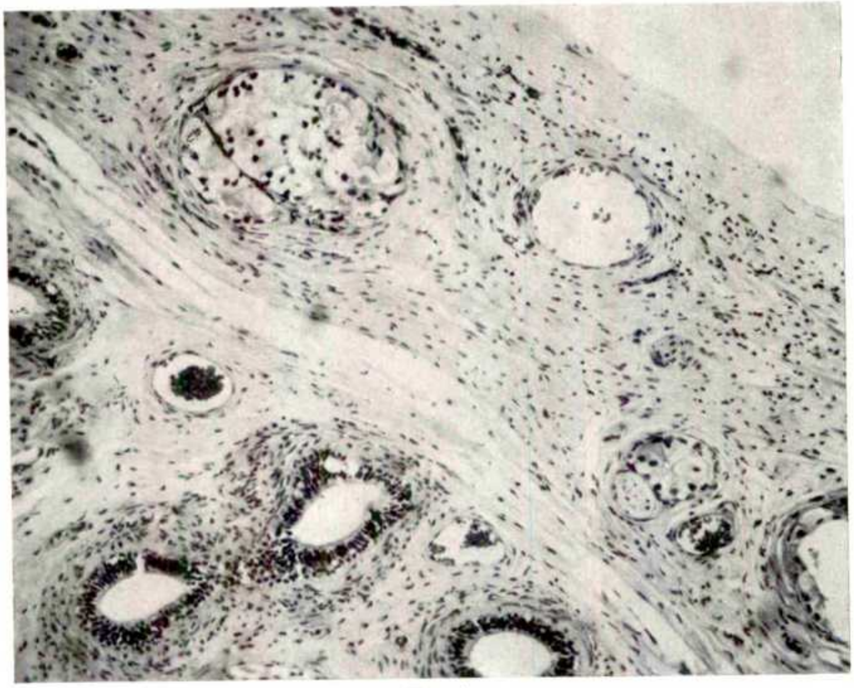

FIG. 4

Intravascular and perineural spread along epididymis. (× 130.)

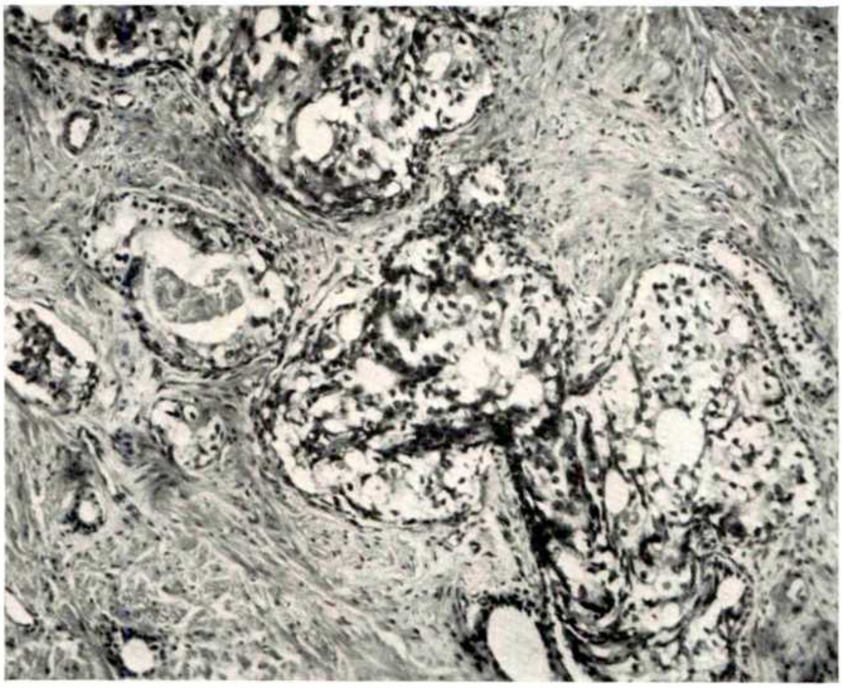

FIG. 5

Residual adenocarcinoma after stilbœstrol therapy for 14 months found at autopsy. (× 130.)

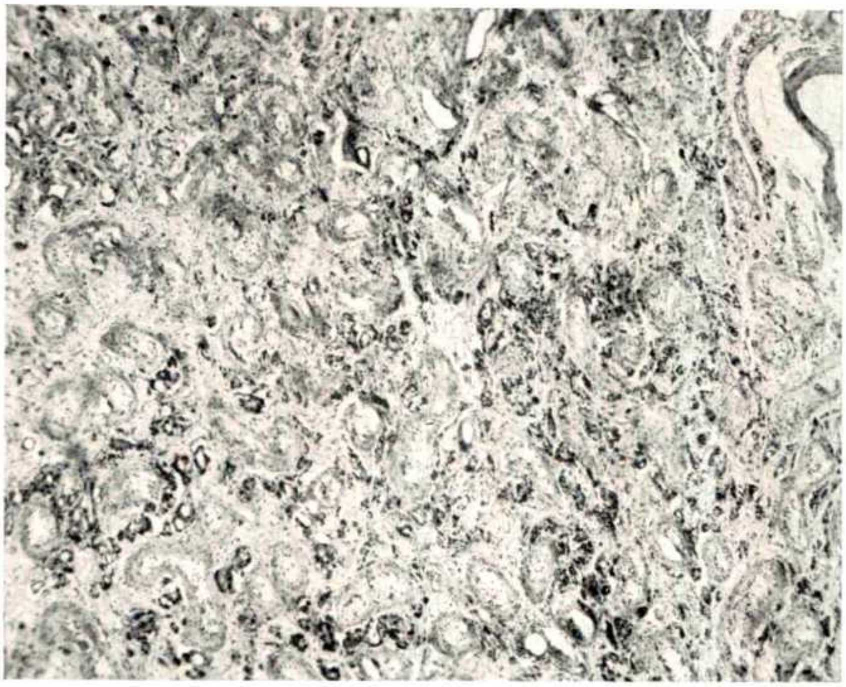

FIG. 6

Scattered groups of metastatic adenocarcinoma among atrophic seminiferous tubules of testis. (× 30.)

The microscopic appearance of this nodule was that of an adenocarcinoma identical to that seen and illustrated in Figure 1. The remaining seminiferous tubules were compressed, completely atrophic and many were hyalinised. The adenocarcinoma also involved the epididymis where isolated perineural invasion was demonstrated (Figs. 3 and 4).

Case 2.—R. B. B., GH 3017.—A 59-year-old white male was first admitted on 23rd February 1949 with complaints of " prostatism " and backache. Rectal examination revealed findings consistent with carcinoma of the prostate. The external genitalia were normal. Bone survey showed generalised osteoblastic metastases. He was given stilbœstrol, 25 mg. three times a day. Biopsy of the fourth lumbar vertebra was reported as metastatic carcinoma, consistent with primary prostatic carcinoma.

Four months after admission a trans-urethral resection was performed because of increasing symptoms of urinary obstruction. Interestingly enough, no evidence of adenocarcinoma was found in the tissue removed. The patient developed hypochromic anæmia. Because of the refractory condition of the disease, stilbœstrol was replaced by estinyl, 1·5 mg. three times a day. Two blood transfusions were administered. He was discharged 8th November 1949.

In the course of his disease, the patient was admitted to the hospital on three occasions. His last entrance was on 16th March 1950, when he complained of weakness, nausea and vomiting, and increasing jaundice. Toxicity to estinyl was suspected. Physical examination revealed icterus, induration of the prostate, but no external genital abnormalities. Laboratory studies showed RBC 4,200,000; WBC 10,400 with 85 per cent polymorphonuclear cells. Blood urea nitrogen was 10 mg. per cent, direct bilirubin 4·6 mg. per cent, indirect 1·3 mg. per cent. Urinalysis showed one plus urobilin and albumin with rare finely granular casts. Again, widespread osteoblastic metastases were noted on a skeletal survey.

During the hospital course he was maintained on intravenous fluids, and the jaundice increased. He vomited coffee-ground material, became gradually weaker, though he never complained of pain. Demise occurred on 12th April 1950, 14 months after his original admission.

Autopsy Report.—The immediate cause of death was a severe hepatitis. There was firmness and whitish-yellow discoloration of the prostate, microscopic sections disclosing foci of residual adenocarcinoma (Fig. 5). Foci of necrotic tumour were present in the bone marrow of the ribs, sternum and vertebræ. The testicles were hypotrophic. On cut section, the left testicle contained a central, opaque, yellow, well-circumscribed nodule, 5 mm. in diameter. Microsections disclosed atrophic hyalinised seminiferous tubules. The interstitium was infiltrated by scattered small groups and islands of adenocarcinoma. Mitotic figures were present (Fig. 6). Other than the prostate, bone marrow, and left testicle, there was no evidence of organ metastasis.

This patient exhibits a rather short course of a disease process, 14 months in all, manifested by widespread metastases to the bones and no organ metastasis save that which occurred in the left testicle, occult in nature.

DISCUSSION

Dissemination of tumour cells may theoretically occur by arterial, venous, and lymphatic routes, as well as by direct extension or via the lumen of the vas deferens (Price and Mostofi, 1957). Arterial embolism has been proven and is associated with widespread metastases (Seamans, 1938). Periductal lymphatic connections between the prostate, epididymis, and testis have been shown investigatively and proven clinically. Secondary testis tumours have a predilection for an interstitial location; the absence of widespread disease and the presence of tumour within the seminiferous tubules is suggestive of intraductal spread within the vas deferens (Howard *et al.*, 1957; Wolf and Madsen, 1968).

SUMMARY

Two unusual cases of testicular metastases from carcinoma of the prostate are reported. In the first patient, the lesion became apparent 10 years after the onset of the disease and was discovered pre-operatively. The metastasis in the second case was found only at autopsy following a relatively short course of the cancerous process and in association with other distant manifestations.

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EVALUATION OF THE URETHRAL ROTATION INVESTIGATION

By STUART L. STANTON[1] and CHARLES D. COLLINS

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THE search for a simple method to distinguish between sphincter weakness and detrusor abnormality in the female with urinary incontinence is still unrewarded. Complicated investigations are often expensive and demand skilled operation and are thereby limited to the larger centres.

Edwards (1971) emphasises these points and describes a technique for distinguishing urethral sphincter weakness from detrusor abnormality by determining the degree of rotation of the urethral axis which results from electrical stimulation of the perineal musculature. This paper reports an evaluation of the urethral rotation test which has been carried out independently in London and Bristol.

Case Material.—Ninety-five patients with urinary incontinence have been investigated in the two centres. The cases were assessed conventionally by history, physical examination, I.V.P., cystoscopy, bacteriological examination of the urine and all those in London and selected cases in Bristol were also investigated with a micturating cystogram.

All the patients were submitted to filling cystometrogram and urethral pressure profile estimation. The cystometrograms were carried out by filling the bladder at a rate of 50 ml./min. through a No. 8 Porges or No. 10 F.G. urethral catheter alongside which was a fine fluid-filled epidural cannula connected to a transducer to measure vesical pressure. Rectal pressure was measured synchronously and both were recorded on a multichannel recorder. The rectal pressure was subtracted from the vesical pressure to give the intrinsic vesical pressure. The technique for pressure profile measurement was essentially that described by Harrison and Constable (1970). On the basis of these tests, the patients were divided into two groups. Those with detrusor dysfunction (26 patients) as demonstrated by the presence on the cystometrogram record of uninhibited bladder contractions either on filling or on standing up and coughing; and those with sphincter weakness (69 patients) as suggested by the history and examination and the finding of a normal cystometrogram.

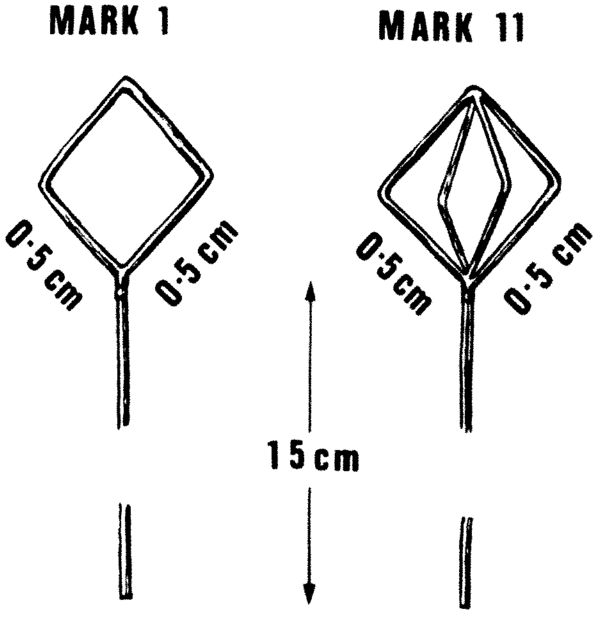

FIGURE: Urethral rotation pins

Method of Urethral Rotation Test.—Two types of urethral rotation-pin were used. The first had a 2-dimensional arrow-head (Mark I) originally used by Edwards and the second had a 3-dimensional four-flanged head (Mark II) which was devised in order to prevent the head falling into the transverse axial plane each time the urethra was pulled forward against the under surface of the pubic symphysis by the pelvic floor contraction which results from perineal stimulation.

Both the original Mark I and modified Mark II rotation-pins (Figure) were used during this evaluation. One of us (C. D. C.) further modified the distal end of the pin to simplify the observations. This did not in any way impair the ability to observe rotation of the urethra.

Perineal stimulation was carried out through needle electrodes at an intensity of 5-10 volts. The radiofrequency pulses were rectangular, of one millisecond duration and at a rate of twenty per second. The rotation-pin was manœuvred within the urethra until the greatest consistent rotational deflection was obtained.

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[1] Senior registrar at St. George's Hospital from 1st June, 1971.

Results.—The results are summarised in the Table. It was impossible to find any significant correlation between the direction and magnitude of rotation and the type of urinary incontinence. Of the 69 patients with stress incontinence, 41 per cent demonstrated a clockwise rotation with the Mark I and 21 per cent with the Mark II rotation-pin. Urethral rotation either failed to occur or occurred in both directions in 44 per cent (Mark I) and 58 per cent of the cases (Mark II). Of the 26 patients with detrusor dysfunction anticlockwise rotation occurred in 27 per cent (Mark I) and 40 per cent (Mark II).

TABLE

Results of Urethral Rotation

Total	Sphincter Dysfunction 69		Detrusor Dysfunction 26	
Arrow	Mark I	Mark II	Mark I	Mark II
Clockwise	26	8	7	4
Anticlockwise	10	8	7	6
Inconsistent/No response	28	21	12	5

DISCUSSION

It was not the authors' intention to investigate the hypothesis of urethral rotation, but only to assess the practical use of the rotation test. The present results do not confirm the consistent results previously reported and do not correlate with those of orthodox standard diagnostic techniques.

A urethral rotation operation has been used to try and correct stress incontinence but in a limited trial at the Institute of Urology it has not been found to be as successful as initially anticipated and the technique has been discontinued.

In conclusion, whilst a degree of urethral rotation can often be demonstrated, the rotation test is considered to be of little diagnostic assistance in differentiating sphincter weakness from detrusor dysfunction and therefore reliance must still be made on conventional methods of assessment.

We would like to acknowledge the help and guidance of Mr J. P. Williams and Mr R. C. L. Fenely and thank Mr K. Wallace for his technical assistance.

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British Journal of Urology (1972), **44**, 602-606

CONCEALED ANTERIOR URETHRAL DIVERTICULUM CAUSING URINARY OBSTRUCTION IN THE MALE CHILD[1]

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Department of Urology, United Bristol Hospitals

CONGENITAL diverticulum of the anterior urethra is an uncommon cause of urinary obstruction in infancy and childhood. Nevertheless, little difficulty is encountered in diagnosis as the outstanding clinical feature is a swelling of the ventral surface of the penis (Kretschmer, 1936). Gross and Bill in 1948 first drew attention to the existence of such diverticula of the anterior urethra without clinical evidence of swelling on the external surface of the penis. Under such circumstances the cause of urinary obstruction may be overlooked, as in 2 of their 3 children, with tragic consequences. We report 2 further cases of concealed, wide-mouthed, diverticula of the anterior urethra diagnosed by urethrography and treated successfully by a simple, one-stage surgical procedure.

CASE REPORTS

Case 1.—J. O., age 6 years, presented with a history of chronic urinary tract infection for which he had received intermittent courses of antibiotics and latterly had been placed on long-term chemotherapy. He was noted by his parents to have persistent dampness of his underpants which were occasionally very wet. No comment was made about the urinary stream. The only significant finding on clinical examination was that his bladder was palpable 2 finger breadths below the umbilicus after micturition. Excretion urography showed a normal upper urinary tract but he was unable to empty his bladder. Micturating cysto-urethrography (Fig. 1) and retrograde urethrography (Fig. 2) demonstrated a wide-mouthed diverticulum in the anterior urethra with a distal flap valve obstruction of the urethral lumen. This finding was confirmed at panendoscopy. On 3.3.70 the diverticulum was explored, (J. P. M.), via a midline perineal incision. The diverticulum was opened in the line of the urethra and the obstructing valvular margin was excised. The incision in the diverticulum was then closed. Following this procedure he has been made aware of a normal urinary stream without straining. A follow-up micturating cystourethrogram demonstrated that the obstruction had been successfully relieved and that the urethra was of a normal calibre (Fig. 3).

Case 2.—R. L., a schoolboy 12 years of age, had never been dry since birth. He had always been required to strain to micturate, the force of the stream was poor and micturition took a long time. In between acts of micturition he had dribbling incontinence. Some 4 years before presentation he had had an excretion urogram performed elsewhere which was reported as normal. Clinical examination was satisfactory and a repeat excretion urogram confirmed a normal upper urinary tract but a large residual urine was present after voiding. The micturating cysto-urethrogram demonstrated an obstruction of the anterior urethra at the peno-scrotal junction with a narrow collapsed anterior urethra distal to this point (Fig. 4). Retrograde urethrography revealed a wide-mouthed anterior urethral diverticulum with a distal flap valve (Fig. 5.)

On 4.3.70 the diverticulum was exposed via a midline perineal incision (M. R.) The diverticulum was incised and traversed to expose the valvular margin at its junction with the urethra. The valvular rim surrounding the mouth of the diverticulum was excised and the incision in the diverticulum closed. Following surgery the boy has been completely dry for the first time in his life and passes a normal urinary stream without effort. Subsequent ascending (Fig. 6) and descending (Fig. 7) urethrography has demonstrated complete relief of the urethral obstruction.

DISCUSSION

Congenital diverticula of the anterior urethra have been classified by Campbell and Harrison (1970) who considered them to occur practically always as blow-out phenomena behind a distal obstruction, notably external meatal stenosis. In the absence of peripheral urethral obstruction the ætiology remains obscure. One of the earliest attempts to explain the origin of diverticula of the anterior urethra was made by Voillemier (1868). He postulated a localised failure of the development of the spongy tissue of the urethra allowing a bulging of the urethra to form a sac on the ventral wall. More recent histological studies have reinforced this concept and Dorairajan (1963) suggested that such diverticula represented local manifestations of widespread developmental derangement of the corpus spongiosum. Suter (1908), considering the embryological development of the urethra, advanced the theory that diverticula of the urethra should be regarded as epidermal pockets communicating with the ventral wall of the urethra. Johnson (1923) discovered cyst-like structures beneath the urethra, with a lining similar to that of the urethra, in an 88 mm. human embryo. He considered that such a cyst might develop a communication with the urethra and thus produce a diverticulum. The appearance of such diverticula suggests

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[1] Based on communication to Royal Society of Medicine, Urology Section, January 1970.

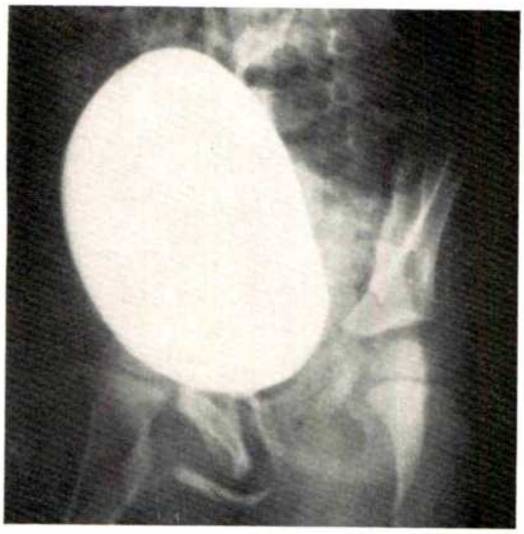

FIG. 1

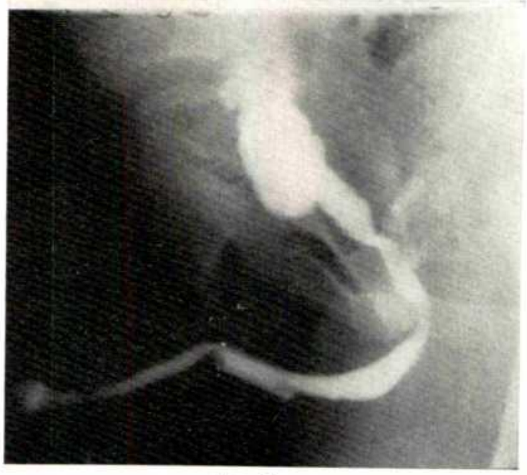

FIG. 2

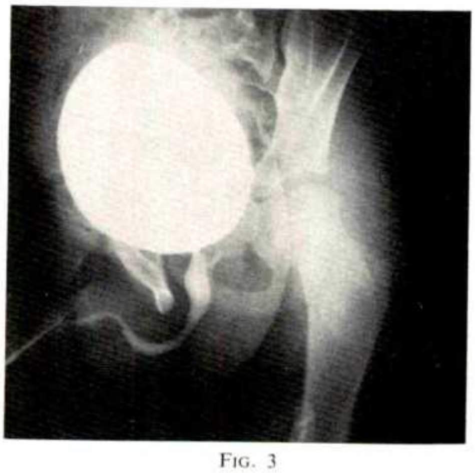

FIG. 3

Fig. 1.—Micturating cysto-urethrogram demonstrating urethral obstruction by a ventrally placed wide-mouthed diverticulum of the anterior urethra. The posterior prolongation of the diverticulum is shown but the anterior lip is not demonstrated (Case 1).

Fig. 2.—Retrograde urethrogram demonstrating the anterior "flap valve" of the diverticulum. (Case 1).

Fig. 3.—Micturating cysto-urethrogram after surgery showing an unobstructed urethra of normal calibre (Case 1).

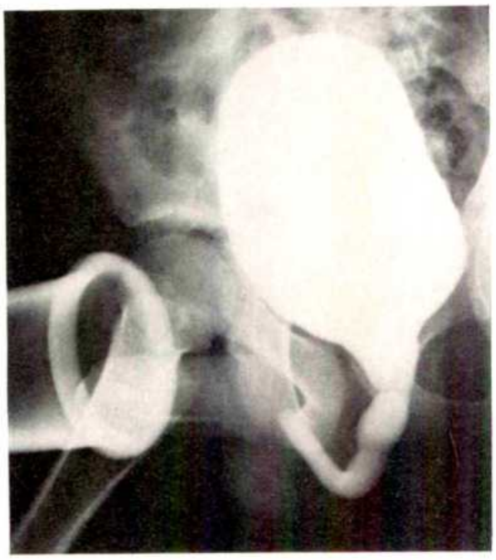

FIG. 4

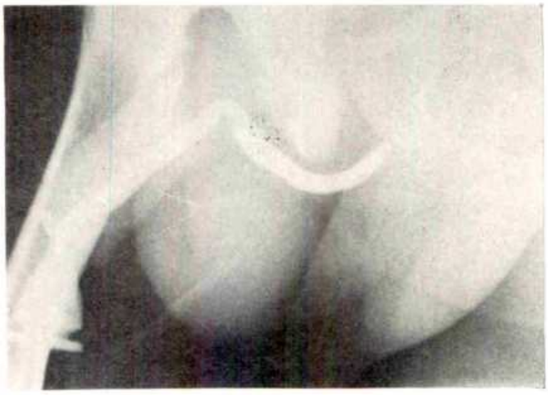

FIG. 5

Fig. 4.—Micturating cysto-urethrogram demonstrating urethral obstruction at the peno-scrotal junction of the anterior urethra with a narrow collapsed anterior urethra distal to this point (Case 2).

Fig. 5.—Retrograde urethrogram showing the distal urethra to be of normal calibre. The shallow ventrally placed diverticulum is filled and the distal obstructing " flap valve " outlined (Case 2).

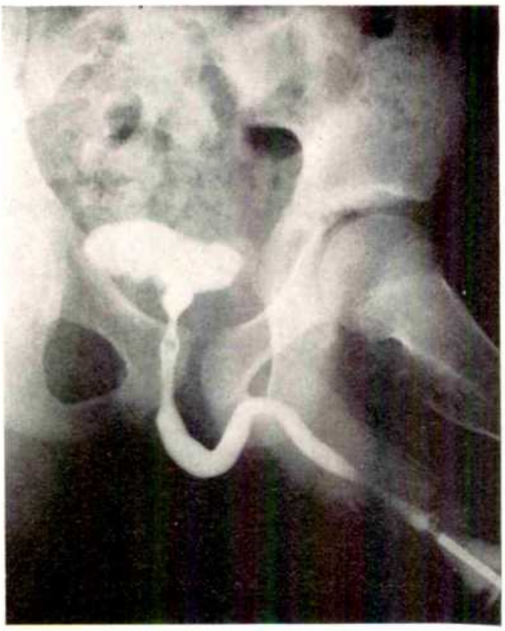

FIG. 6

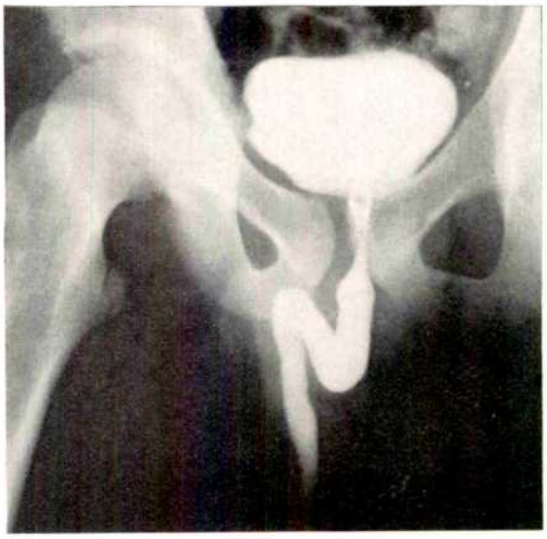

FIG. 7

Fig. 6.—Retrograde urethrogram after surgery demonstrating a normal calibre urethra (Case 2).

Fig. 7.—Micturating cysto-urethrogram after surgery demonstrating relief of the urethral obstruction (Case 2).

an abortive duplication of the urethra (Williams, 1958). Campbell (1970), also considers that these diverticula may be a limited or modified from of accessory urethral canal.

The anterior urethral diverticula encountered in our patients were in each case oval shaped, ventrally placed pouches lying with their long axes parallel to the floor of the urethra at the peno-scrotal junction. The mouth of the diverticulum had a valvular rim, the distal lip of which was displaced upwards against the roof of the urethra on micturition in such a way as to impede the flow of urine in the anterior urethra. This mode of urinary obstruction was recognised by Watts (1906) who considered that the majority of valves described in association with anterior urethral diverticula were merely secondary formations due to undermining of the urethral wall by the diverticulum as it increased in size. He noted in his review that a similar valvular obstruction may occur in acquired diverticula resulting from traumatic rupture of the urethra.

Anterior urethral valves, without an associated diverticulum, causing urinary obstruction, have been noted on the ventral wall of the urethra in the region of the peno-scrotal junction (Williams, 1958; Hope *et al.*, 1960; Waterhouse and Scordamaglia, 1962). It is possible that proximal turbulence of the urinary stream associated with such a valve may subsequently give rise to a shallow diverticulum of the urethral floor.

Dribbling incontinence of urine was a prominent complaint in both of our patients. In the older child straining on micturition with a poor urinary stream suggested bladder outflow obstruction. In the younger child superimposed urinary infection was the dominant feature but a palpable bladder after micturition made exclusion of an underlying obstructive lesion imperative. In the absence of a palpable swelling on the underside of the penile urethra the diagnosis of " concealed " anterior urethral diverticulum depends largely upon urethrography by either the ascending or descending routes.

The urethrographic features of this type of diverticulum have been discussed by Stephens (1963) and Williams (1968) and were well demonstrated in our 2 patients. Williams emphasised that micturition or expression urethrography will outline the shallow diverticulum and demonstrate the obstructive effect of the distal lip. The anterior urethra distal to the valve appears narrow on descending urethrography but retrograde or injection urethrography shows the distal urethra to be normal in calibre. The latter investigation in our patients demonstrated both the valve and the posterior prolongation of the diverticulum. We consider that urethrography by both the descending and ascending routes is mandatory for the diagnosis of this anomaly as either investigation alone may fail to demonstrate the nature of the obstruction.

The treatment of wide-mouthed anterior urethral diverticula has usually involved a two-stage urethroplasty, as excision of the diverticulum leaves only a strip of the roof of the normal urethra which cannot be closed without narrowing (Williams, 1968). Gross and Bill (1948) concluded that " It is not necessary—and indeed undesirable—to remove the diverticulum itself ". They demonstrated that the urethral obstruction can be effectively relieved by removal of the associated valve. In their patient, a boy of 9 months, the valvular roof was removed with a ring punch inserted via a perineal incision into the diverticulum itself. The success of this simple, one-stage procedure encouraged us to use this approach in the surgical treatment of our 2 patients which we recommend as a simple and satisfactory alternative to staged urethroplasty in the management of this condition.

SUMMARY

Two male children with " concealed " anterior urethral diverticula causing urinary obstruction are presented. The ætiology and diagnosis are discussed and a simple, successful, one-stage operation described.

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THE RÔLE OF CORPUS-SAPHENOUS BY-PASS IN THE TREATMENT OF PRIAPISM

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FOLLOWING the introduction of corpus-saphenous by-pass for the treatment of persistent priapism by Grayhack, *et al.* (1964), there have been a number of reports of its successful use. We present two further cases of priapism treated by corpus-saphenous by-pass, and include pre- and post-operative corpus cavernosograms. The rôle of by-pass in the treatment of priapism is defined, and some aspects of the cases reported previously are summarised.

CASE REPORTS

Case 1.—A 55-year-old white male was admitted for investigation of epigastric pain. He had undergone surgery for peptic ulceration on three occasions between 1955 and 1961. Following a rectal examination he developed an erection which persisted and which he concealed for 24 hours. The glans penis and corpus spongiosum were not involved in the priapism. The erection failed to respond to Ethyl Chloride sprays, ice-packs and sedation. No abnormality was found in the patient's blood film, white cell count or platelet count. A sickle cell test was negative. Radiographs of the lumbar spine and an intravenous pyelogram were normal. A spinal anæsthetic was given and the patient was catheterised to relieve retention of urine. The right corpus cavernosum was aspirated, resulting in a temporary detumescence. Sixty hours from the onset of priapism, corpus-saphenous by-pass was performed. A pre-operative corpus cavernosogram (Fig. 1) by unilateral injection of Meglumine iothalamate 60 per cent demonstrated filling of both corpora. A unilateral by-pass was therefore constructed by anastomosis of the proximal end of the divided long saphenous vein to a 1 cm. diameter window cut in the side of the right corpus cavernosum, as described by Grayhack *et al.* (1964). 6/0 Ethiflex was used to anastomose the vein to the corpus, and a continuous heparin infusion was administered through a fine cannula inserted into the cavity of the left corpus. A cavernosogram was obtained at the completion of the operation (Fig. 2). Almost complete detumescence was obtained, although the penis remained œdematous. The heparin was discontinued after 5 days. The area around the cannula had become infected, as had the wound at the base of the penis. Following drainage of pus from the wound and treatment with antibiotics, the infection subsided but the penis remained indurated. On the 9th post-operative day a further cavernosogram was performed with the patient's consent (Fig. 3). Following discharge from hospital, the penis remained indurated and erection had not occurred when seen at follow-up 6 months later.

Case 2.—A 29-year-old white male awoke with an erection which persisted. Intercourse had occurred during the previous night. On admission, no cause could be found for the priapism which did not involve the glans or corpus spongiosum. No abnormality was found in the patient's blood film, white cell count or platelet count. A sickle cell test was negative. Radiographs of the lumbar spine and pelvis were normal. Thirty-three hours after the onset of priapism, a corpus cavernosogram was performed prior to operation (Fig. 4). Contrast medium injected into the right corpus did not flow freely into the left corpus. However at operation, when the right corpus was incised, bilateral flaccidity ensued. A unilateral (right) corpus saphenous shunt was therefore constructed and a post-operative cavernosogram (Fig. 5) demonstrated a functioning by-pass. Complete detumescence did not occur immediately although the penis became flaccid. Systemic heparin was commenced, but 48 hours later, a scrotal hæmatoma developed and the heparin was discontinued. The hæmatoma was evacuated and a further cavernosogram performed on the 4th post-operative day demonstrated the by-pass to be patent. On the 7th post-operative day the patient obtained a near normal erection, and a corpus cavernosogram on the 9th post-operative day failed to demonstrate the by-pass (Fig. 6). When seen in follow-up 4 weeks after operation, the patient had had normal sexual intercourse on several occasions.

DISCUSSION

Grayhack *et al.* reported the successful use of corpus-saphenous by-pass for the treatment of priapism in 1964. Since then there have been a number of reports of its use. (Garrett and Rhamy, 1966; Grace and Winter, 1968; Kandel *et al.*, 1968; Howe *et al.*, 1969; Martin *et al.*, 1969; Martinez *et al.*, 1969; Eddie and Brock, 1970; Hamm and Waterhouse, 1970).

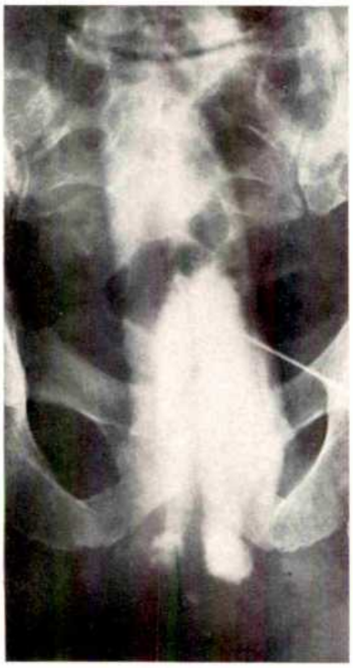

FIG. 1

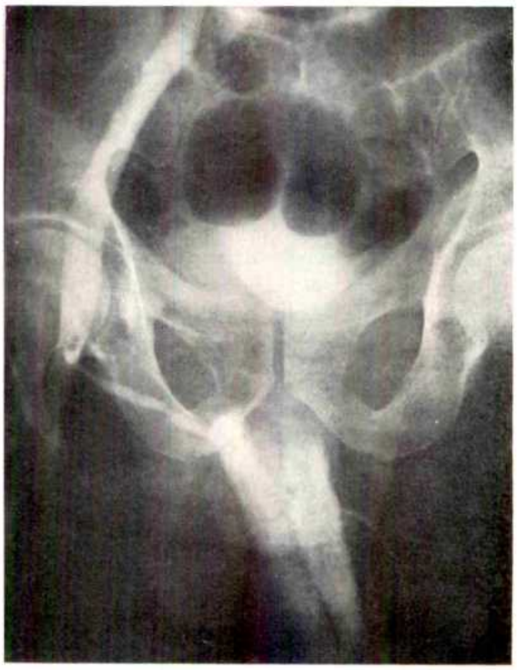

FIG. 2

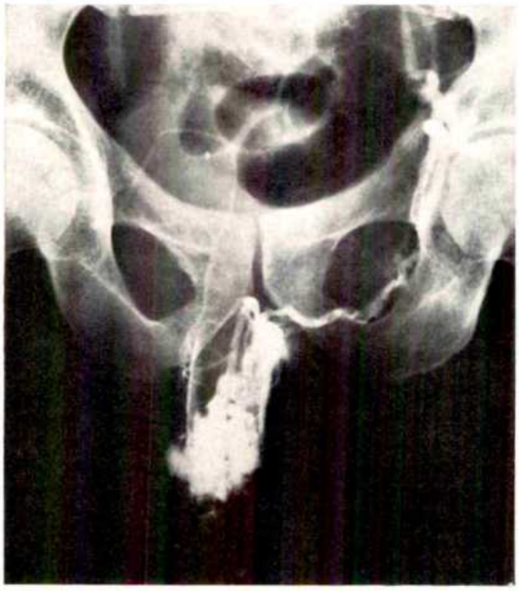

FIG. 3

Fig. 1.—Case 1.—Pre-operative cavernosogram demonstrating stasis of contrast in the corpora cavernosa with free communication between the corpora.

Fig. 2.—Case 1.—Corpus cavernosogram obtained at end of operation. Contrast injected into the left corpus demonstrates detumescence and a patent right corpus-saphenous shunt.

Fig. 3.—Case 1.—Cavernosogram obtained on 9th post-operative day. The corpora are no longer draining through the shunt, but through a patent deep dorsal vein of penis, mainly into the left pudendal vein.

Hinman (1960) suggests a working hypothesis for the ætiology of idiopathic priapism, and states that failure to relieve venous stasis in the corpora promptly may lead to fibrosis in the corpora and impotence. The aim of corpus-saphenous by-pass is not only to induce detumescence, but also, by relieving stasis in the corpora, to avoid fibrosis and ensure return of the penis to

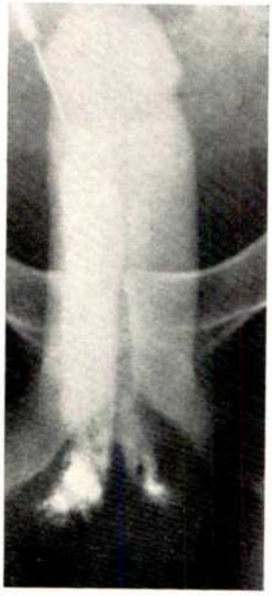

FIG. 4

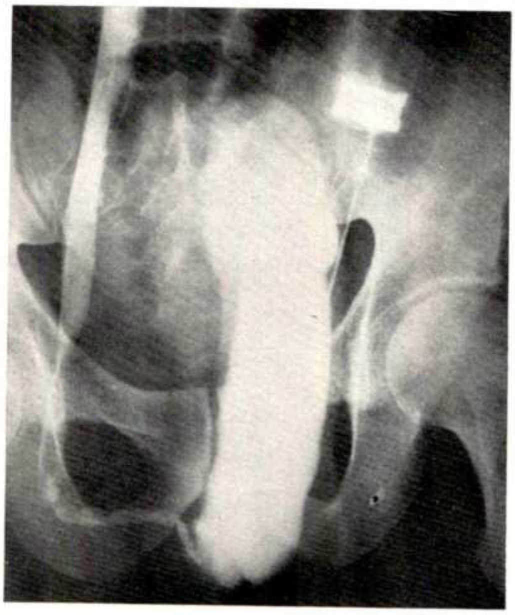

FIG. 5

Fig. 4.—Case 2.—Pre-operative corpus cavernosogram, injection into right corpus. The left corpus fills only to a slight extent at its base suggesting poor communication with the right corpus. No exit of contrast from the corpora is seen.

Fig. 5.—Case 2.—Corpus cavernosogram performed on completion of the operation. The patent right corpus saphenous by-pass is shown. Penis is flaccid but complete detumescence has not yet occurred.

Fig. 6.—Case 2.—Cavernosogram performed on the 9th post-operative day. The by-pass is no longer shown. The cannula used to inject contrast is seen in the right corpus. The deep dorsal vein of the penis is visualised. Contrast medium passes into the prostatic plexus and into the internal pudendal veins.

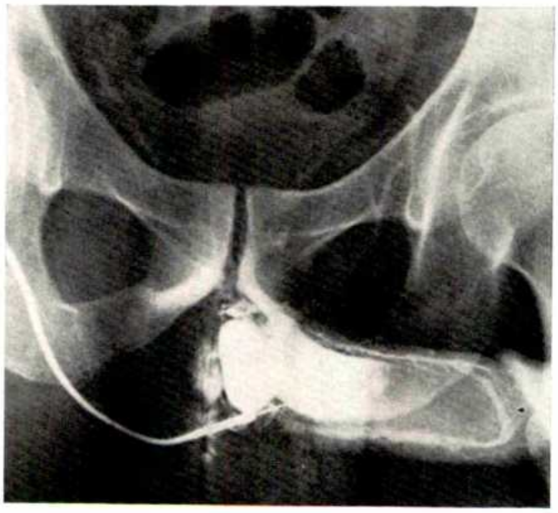

FIG. 6

normal sexual function. Hence, several authors have urged early or even urgent surgical intervention (Garrett and Rhamy, 1966; Kandel *et al.*, 1968; Howe *et al.*, 1969; Eddie and Brock, 1970). Others (Grace and Winter, 1968; Hamm and Waterhouse, 1970) point out the variable natural history of priapism and recommend a trial of conservative measures before venous by-pass is undertaken.

Several authors have pointed out the purely temporary patency of the corpus-saphenous shunt (Garrett and Rhamy, 1966; Martinez *et al.*, 1969). The by-pass tends to thrombose as an alternative venous drainage from the corpora opens. The re-establishment of an alternative

TABLE

Author	Duration of Priapism Before By-pass	Potent
Grayhack *et al.* (1964) (1 patient)	10 days	Yes
Garrett and Rhamy (1966) (5 patients)	4 days	Yes
	36 hours	Yes
	4 days	Yes
	72 hours	?
	32 hours	Yes
Grace and Winter (1968) (2 patients)	6 days	Yes
	48 hours	Yes
Kandel *et al.* (1968) (1 patient)	10 days	Yes
Martinez *et al.* (1969) (1 patient)	16 days	Yes
Martin *et al.* (1969) (3 patients)	6 days	No
	72 hours	Yes
	21 hours	Yes
Howe *et al.* (1969) (5 patients)	13 days	No
	80 hours	Yes
	36 hours	Partial
	72 hours	No
	20 hours	No
Eddie and Brock (1970) (2 patients)	15 days	No
	48 hours	No
Hamm and Waterhouse (1970) (9 patients)	4 days	?—follow-up too short
	16 days	?—No follow-up
	6 days	No—at 1 month
	5 days	No—at 2 months
	8 days	No—at 6 months
	12 days	Yes
	11 days	Yes
	4 days	No—at 6 months
	5 days	Yes
Wellwood *et al.* (1972) (2 patients)	60 hours	No—at 6 months
	33 hours	Yes

venous drainage would seem to occur between the 6th and 8th post-operative days. Howe *et al.* (1969) record the return of priapism following the clotting of a by-pass on the 3rd post-operative day, and Eddie and Brock (1970) noted return of priapism on the 6th post-operative day due to obstruction of the by-pass. In the second patient described here normal erection occurred on the 7th post-operative day, suggesting closure of the by-pass, and Martinez *et al.* (1969) also record normal erection on the 6th post-operative day. Kandel *et al.* (1968) report closure of a bilateral corpus-saphenous by-pass on the 6th post-operative day and Martin *et al.* (1969) record clotting of a by-pass on the 8th post-operative day without return of priapism. In both the patients we present, radiographs confirmed closure of the by-pass without return of priapism by the 9th post-operative day (Figs. 3 and 6).

Corpus cavernosography is best performed using an image intensifier and television screening, either in the operation theatre or immediately pre-operatively in the X-ray department. An automatic exposure device is helpful to minimise gonadal radiation by avoiding the need to repeat technically unsatisfactory films. Fluoroscopy enables the degree of cross-flow of contrast to be visualised so that unilateral or bilateral injections can be made as indicated. The contrast medium meglumine iothalamate 60 per cent combines low viscosity with good radio-opacity so that injection can be made through a 20-gauge or smaller needle.

The use of pre-operative cavernosography as advocated by Grayhack *et al.* (1964) and Martin *et al.* (1969) to show the degree of communication between the corpora may not be essential. Even if the communication appears poor angiographically, as in our second patient (Fig. 4), bilateral flaccidity may be achieved with a unilateral shunt. The successful use of bilateral shunts has been recorded by Grace and Winter (1968); Kandel *et al.* (1968); Martinez *et al.* (1969); and Hamm and Waterhouse (1970). Probably the indication for a bilateral by-pass is failure of unilateral drainage of the corpora to achieve detumescence.

Fibrosis in the corpora and impotence may result from prolonged venous stasis (Hinman, 1960). In the first patient recorded here some of the residual induration in the penis may have been due to infection. The Table relates the duration of priapism before operation to subsequent potency. Numbers are small, but the figures do not indicate that urgent by-pass in the treatment of priapism is mandatory, a view supported by Grace and Winter (1968). Five of the 7 patients treated by by-pass within 48 hours regained potency, but 5 of the 8 patients treated 1 week or more after the onset of priapism also regained potency (Table). Other factors may affect the return of potency including infection of the corpora, and age of the patient.

SUMMARY

Two patients with idiopathic priapism are described. Some aspects of the use of surgical by-pass are discussed. The obstruction to venous return from the corpora cavernosa in priapism, its treatment by venous by-pass, and the ultimate development of a new venous drainage from the corpora, are demonstrated by cavernosography. Even when priapism has existed for a number of days, surgical venous by-pass will induce detumescence and may preserve potency.

We would like to thank Mr A. Mulholland and Mr A. E. Thompson under whom the first patient was admitted and Mr K. E. D. Shuttleworth under whose care the second patient was admitted, for their kind permission to record these cases.

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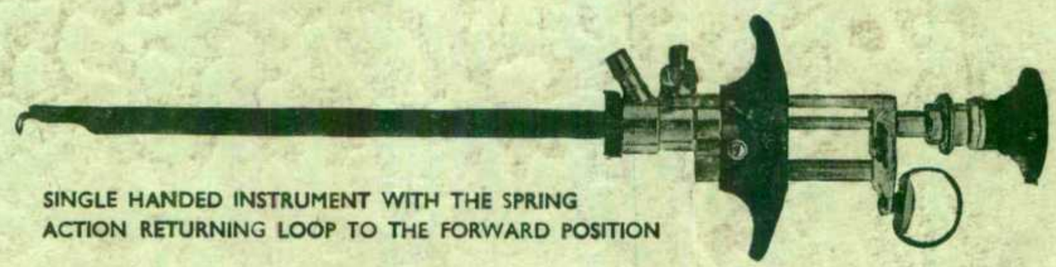

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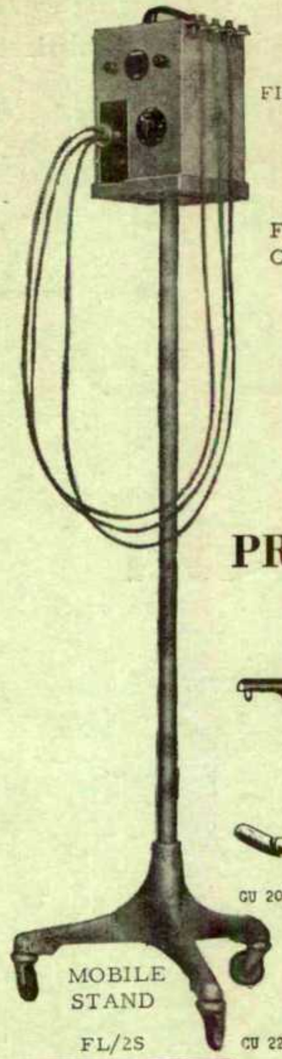

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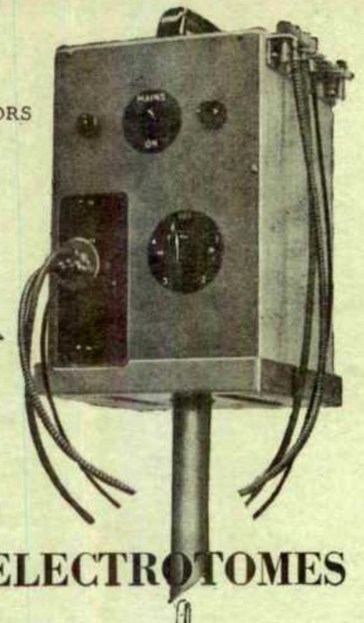

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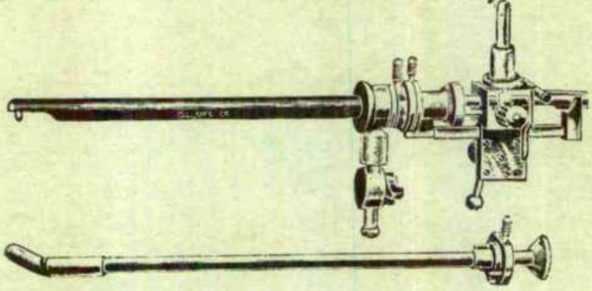

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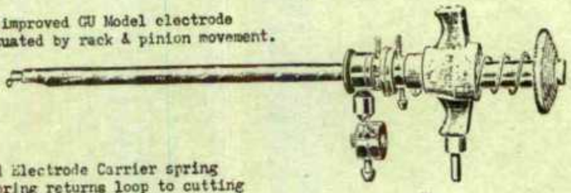

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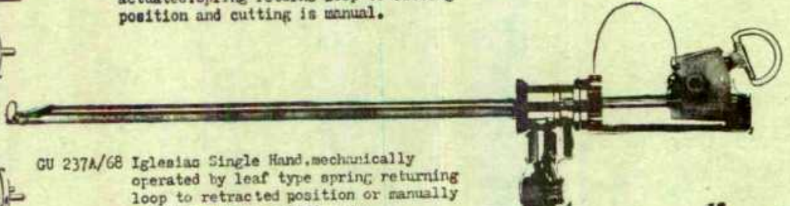

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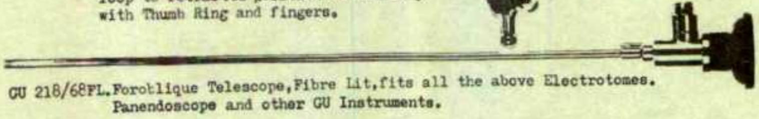

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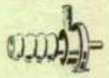

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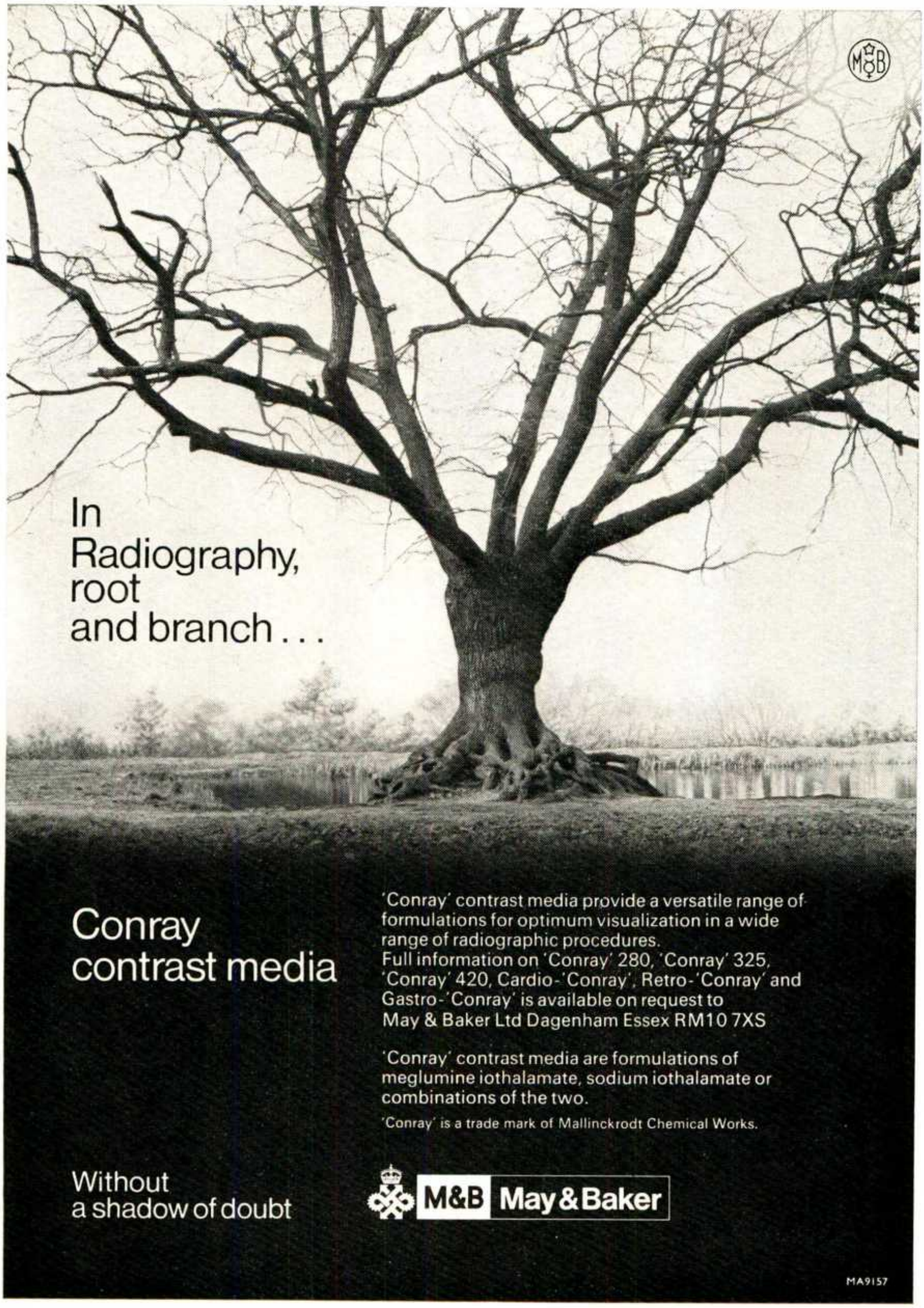

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(1) *Postgrad med J*, (1971), (September Supplement), *47*, 7.
(2) *Brit med J*, (1969) *i*, 541.
(3) Leading Article, *Brit med J*, (1969), *i*, 525.

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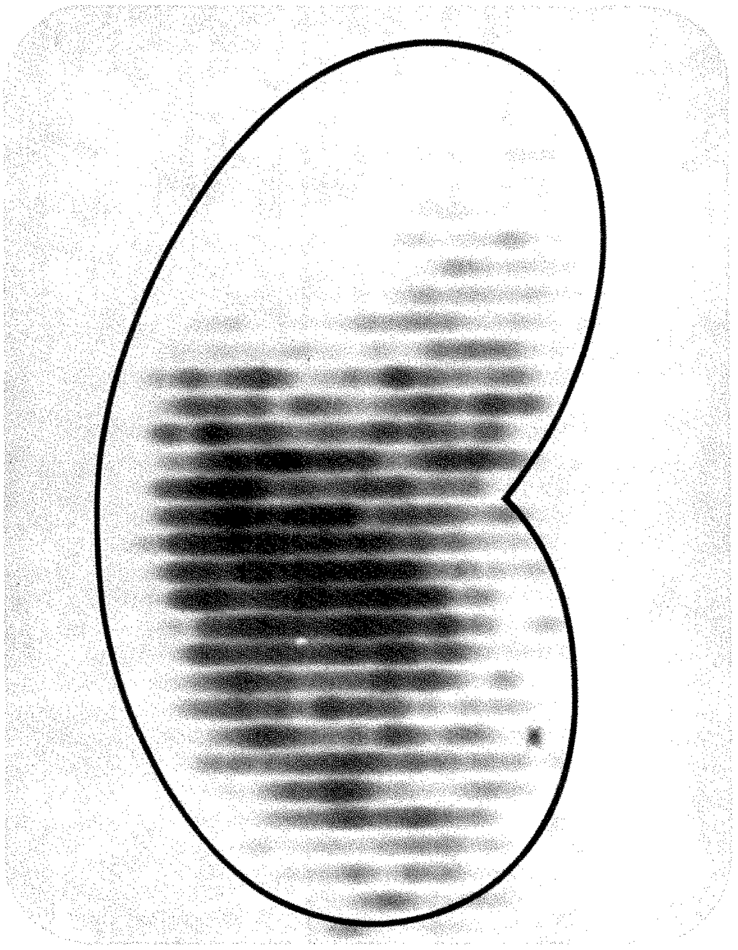

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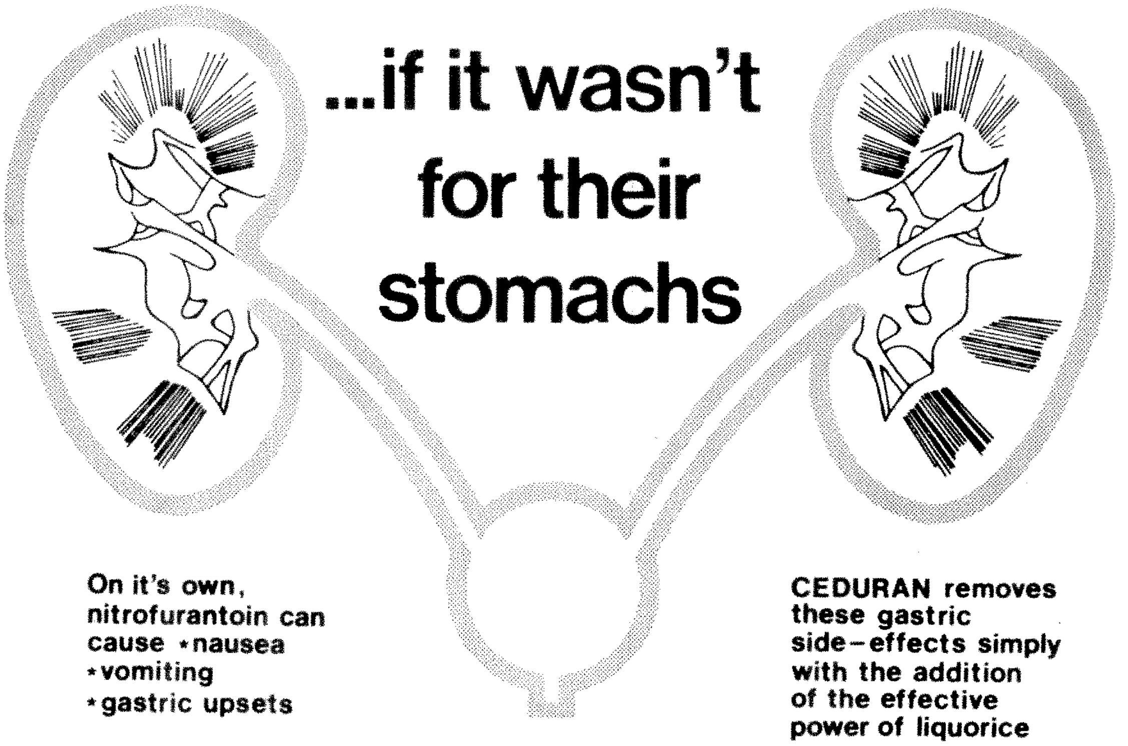

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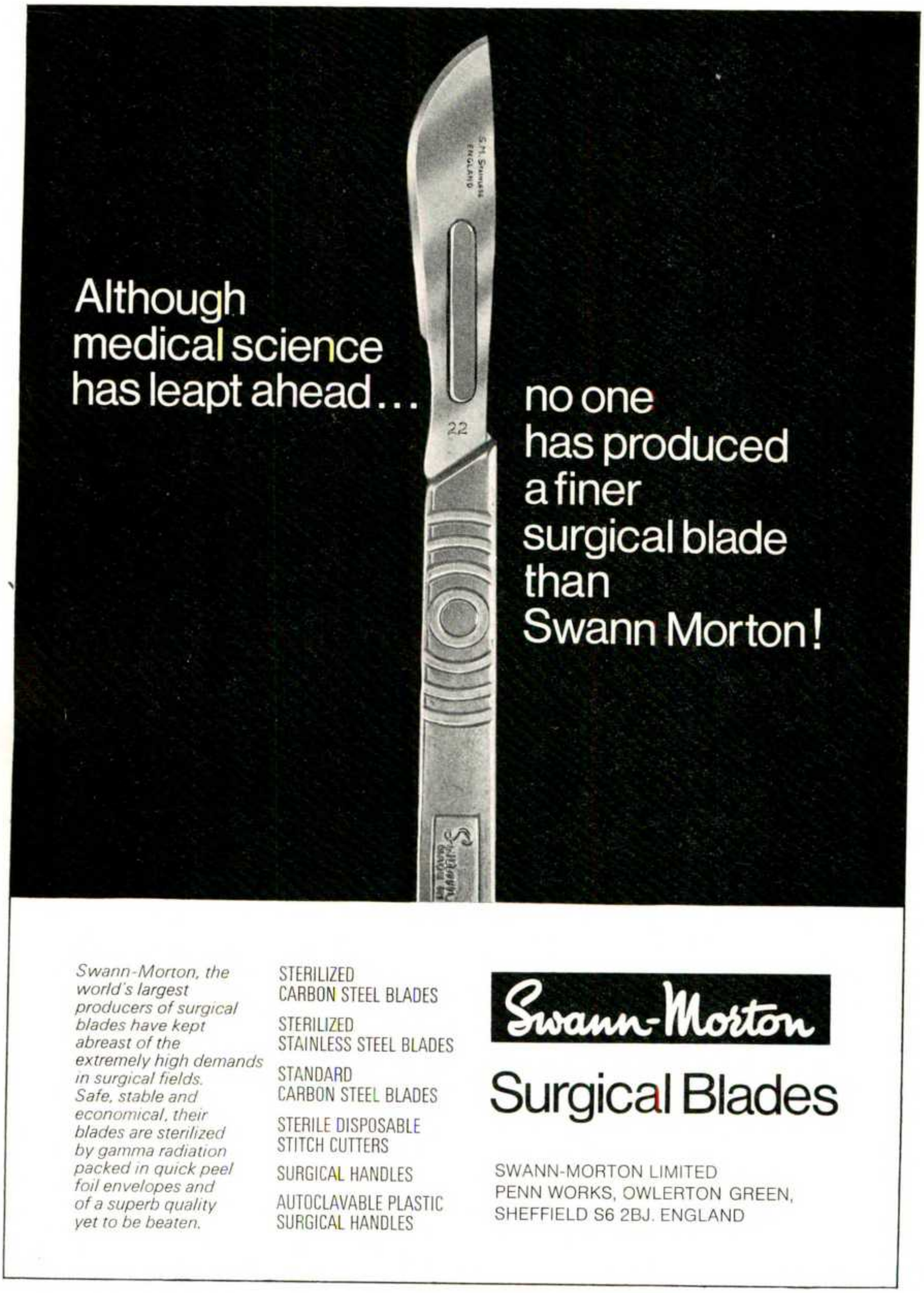

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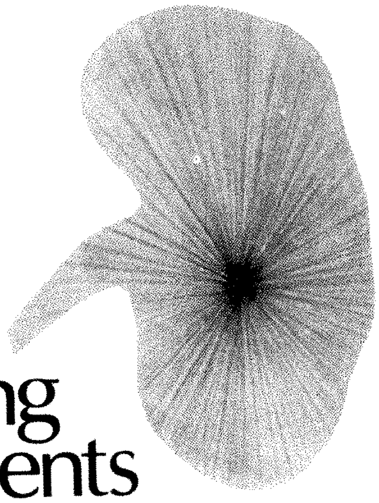

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1. *Clin Sci*, (1964), 27, 417.
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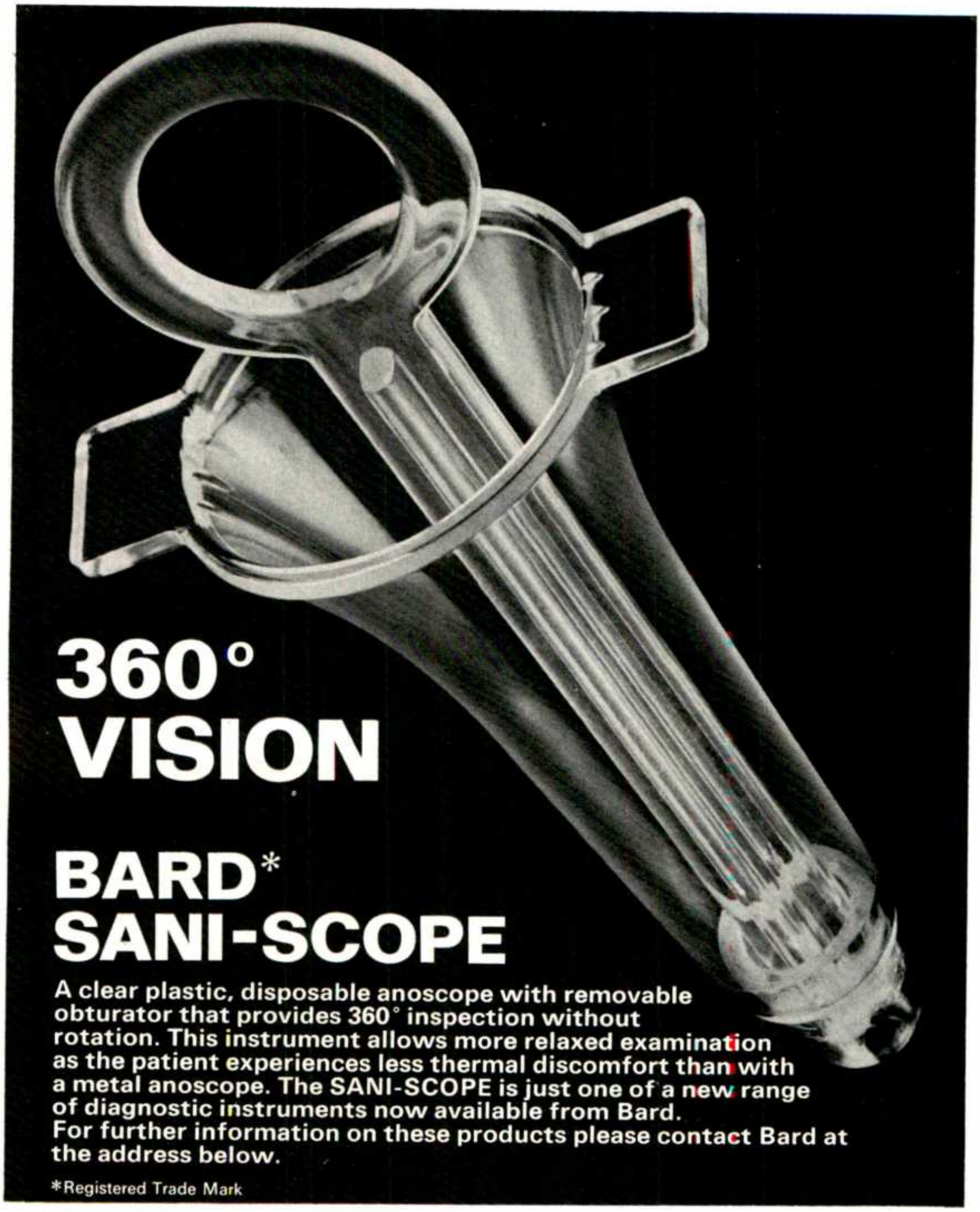

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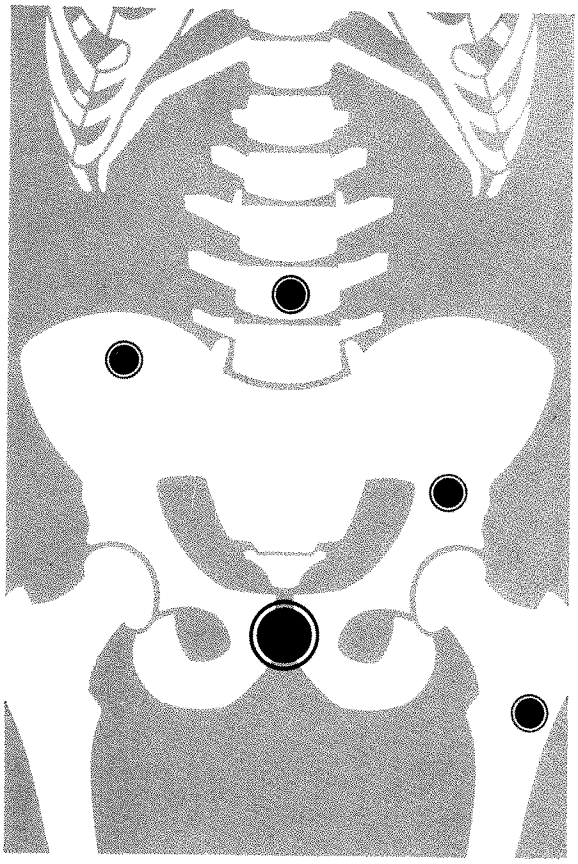

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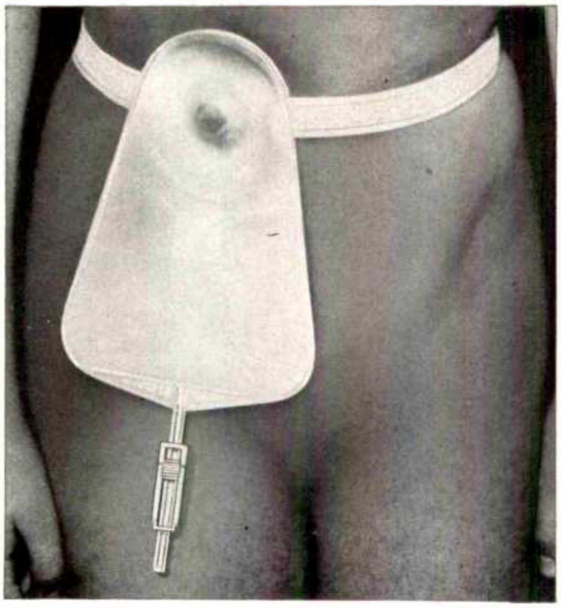

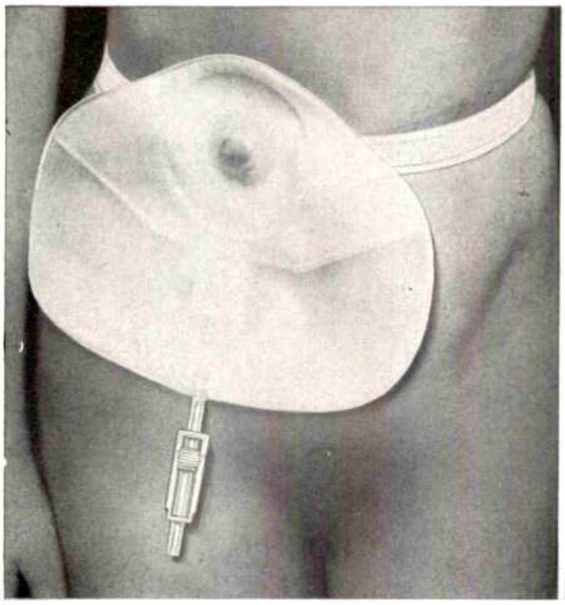

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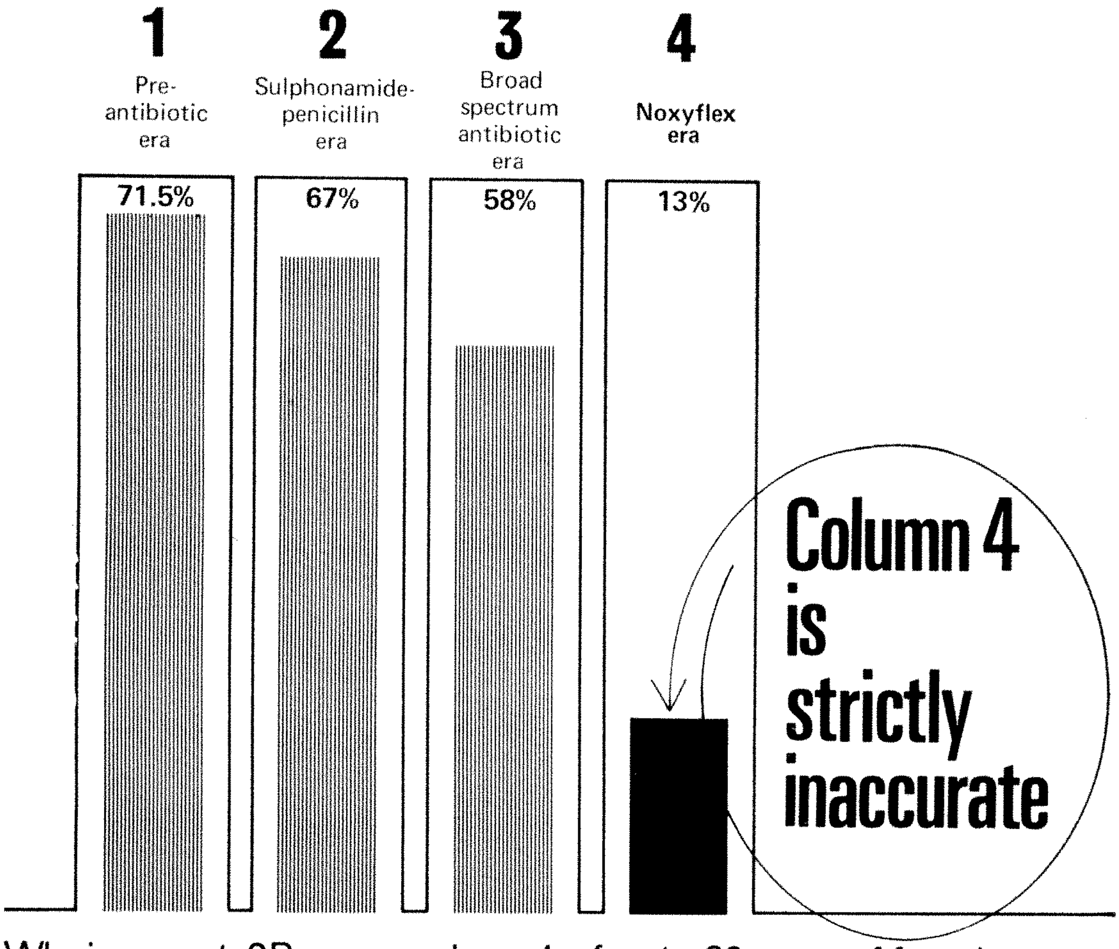

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Die Bedeutung des Werkes wird duch die Tatsache offensichtlich, daß das Harnsteinleiden zu den Volkskrankheiten zählt. Spezialisten auf dem Gebiet der Harnsteinforschung behandeln die Problematik der Entstedung der Harnsteine und Zusammensetzung sowie deren verschiedene Formen. Weiter werden die sich aus den Steinanalysen ergebenden therapeutischen Konsequenzen mit der nötigen Vorsicht abgehandelt.
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1. *E.D.T.A. Proceedings*, VOL VI; (1969). 2. *British Journal of Urology*, (1970) **42**; 246. 3. *British Medical Journal*, (1969) **IV**; 717. 4. *British Journal of Urology*, (1970) **42**; 590. 5. *Lancet*, (1963) **ii**; 1143. 6. *J.clin.Path.*, (1964) **17**; 362. 7. Paper presented to the Dutch Ophthalmological Congress, Amsterdam, 1970. 8. *Lancet*,(1970) **ii**; 1116. 9. *J.clin.Path.*,(1964) **17**; 355. 10. *Arch.Dis.Childh.*, (1965) **40**; 235.

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2. Sack, E. et al. (1962). New Engl. J. Med. **266**, 541.
3. Andersson, L. (1964). Acta Chir. Scand. **127**, 552.
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1. Brit. Med. J., 1972, *3*, 13.
2. Brit. J. Clin. Pract, 1972, *26*, 341.

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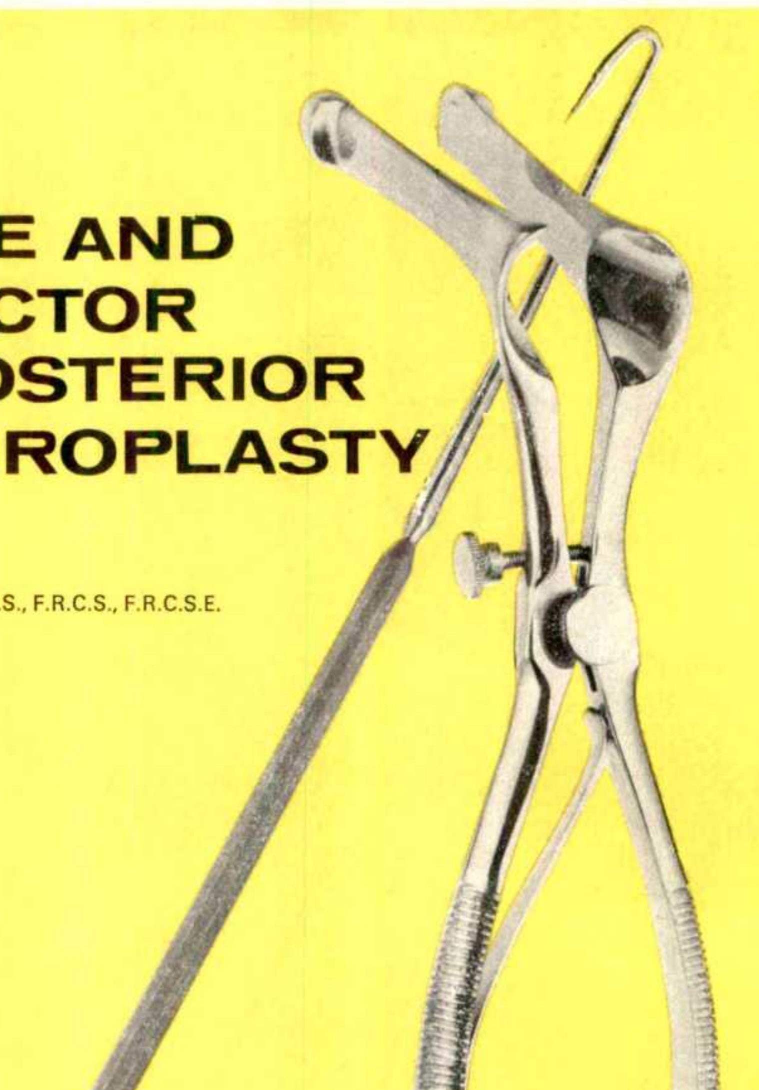

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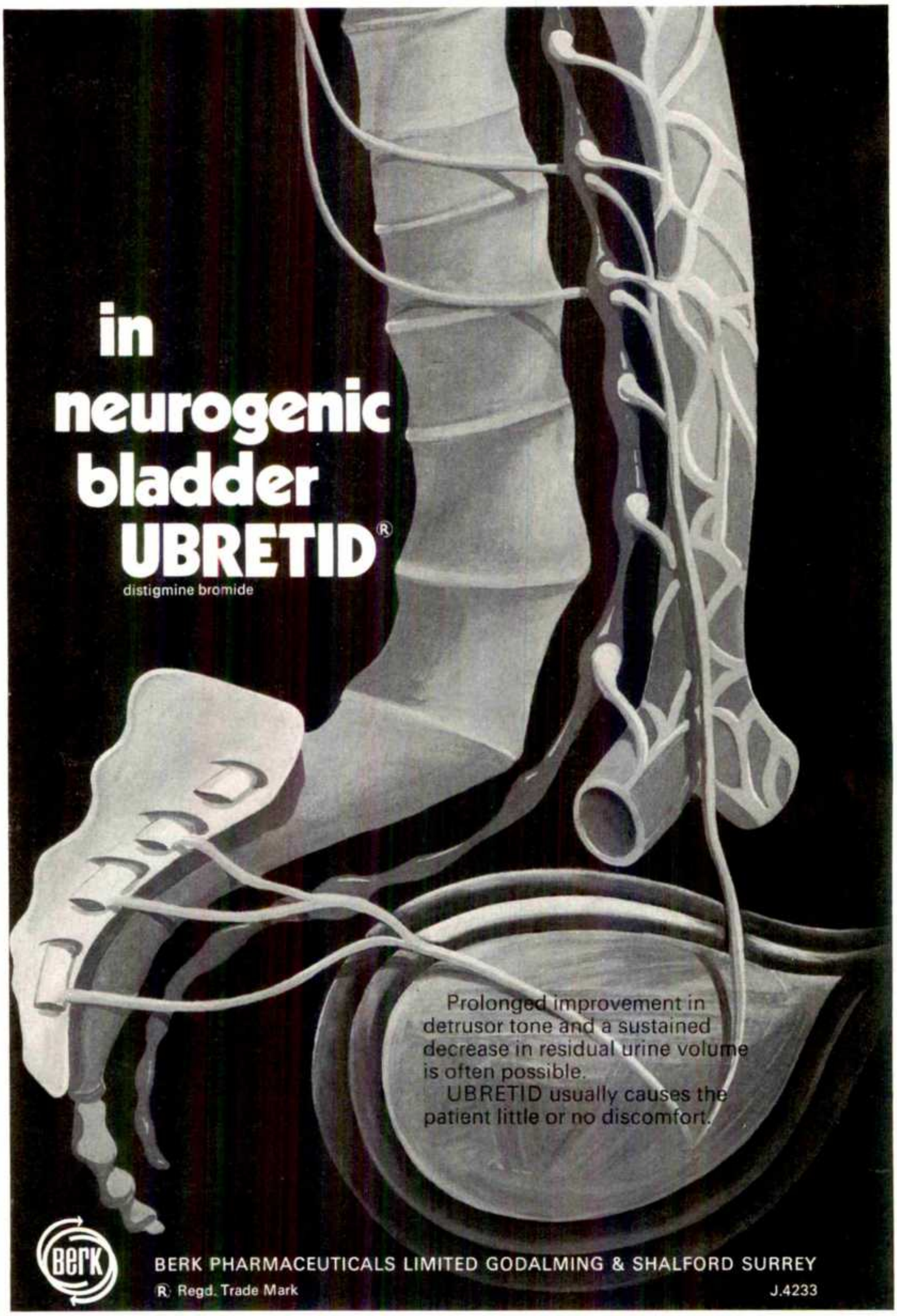

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EDITORIAL CHANGES

It is sad to report that this number completes the last volume of the *British Journal of Urology* which will be edited by Mr J. D. Fergusson: through the past six years as Editor and the preceding seventeen as Assistant Editor he has guided the Journal through its most successful phase of expansion. The volumes have become progressively larger, they have reached more readers in more countries and, as a result, a hugely increased number of papers are submitted for publication from all parts of the world. The reading, criticism and selection of these papers has placed an exceptionally heavy burden on the Editor, but in spite of his many other responsibilities in the urological field he has carried this very largely himself and so efficiently that no one has questioned his good judgement in the choice of those reaching publication. During his time we have also seen the production of a number of supplements, issued free to subscribers, adding greatly to the service provided by the Journal.

The last two years have been particularly difficult because of change in the publisher's arrangements. With the departure last year of Miss Gardner, one of the mainstays of the organisation in Edinburgh, and the amalgamation of Livingstone's with the larger Longman Group, resulting in a move of the publishing activity from Edinburgh to London, many problems have arisen. Happily, Mr Fergusson has been successful in straightening most of these before handing over to his successor, Mr Keith Yeates of Newcastle, whom we welcome as the new Editor confident that he has plans for innovations which will nevertheless preserve the traditions established for management of the Journal which have proved so successful in the past. Mr Fergusson's advice will continue to be available from his new position of Consulting Editor.

Mr Basil Page and Mr Selby Tulloch remain as Assistant Editors in London and Edinburgh while Mr Geoffrey Chisholm is added to the team in London.

On the Committee side Mr A. W. Badenoch has resigned from the Chairmanship of the Editorial Committee and I shall have a difficult task in emulating his wise direction of policy. Mr Hugh Kinder takes over as Treasurer with the knowledge that the financial position is sound if not exciting.

D. Innes Williams,
Chairman of the Editorial Committee.

THE BRITISH ASSOCIATION OF UROLOGICAL SURGEONS

THE TWENTY-EIGHTH ANNUAL GENERAL MEETING was held in the Lecture Theatre, Physics Concourse, University of Newcastle upon Tyne, on WEDNESDAY, 5th JULY 1972 at 3 p.m.

The President, Mr J. D. Fergusson, was in the Chair.

1. **Minutes** of the Annual General Meeting held on 23rd June, 1971, and of the Special General Meeting held in Oxford on 9th October, 1971 which had been circulated were taken as read and signed as correct.

2. **Death.** The meeting learned with regret of the death of Dr Keith Kirkland and stood in tribute to his memory.

3. **Election of New Members.** The following were elected Full Members on the nomination of the Council:

Mr J. R. G. Bastable, York; Mr G. J. Coorey, Sydney, Australia; Mr J. G. Coxon, Halifax; Mr R. F. Deane, Glasgow; Mr M. H. Devereux, London; Mr W. H. Garvie, Aberdeen; Mr H. W. Gowland, Wellington, New Zealand; Mr A. Mulholland, London; Mr M. R. G. Robinson, Pontefract; Dr M. A. Zia, Lahore, Pakistan.

It was pointed out that Dr Zia's application for Full Membership had been approved by the Council before Pakistan had withdrawn from the British Commonwealth, and his election was therefore confirmed.

4. **Report of Council for 1971/72.** The report of Council for 1971/72, which had been circulated, was received and adopted.

The President stated that Mr A. R. C. Higham had been elected a Senior Member. He also reported that the Urological Prize had been awarded to Mr Lynn Edwards.

5. **Report of the Honorary Treasurer and Balance Sheet to 31st December 1971.** The audited accounts for the year 1971, which showed a deficit on the year's working of £411·67, were presented by the Honorary Treasurer and approved.

6. **Amendments to the Rules.** On the recommendation of the Council it was agreed that the following amendments should be made to the Rules:

Rule 3, "Membership": Members shall be medical practitioners, fully registered in Great Britain, the Commonwealth, the Republic of Ireland or South Africa (except in the case of Honorary Members, Corresponding Members and Affiliated Members) and concerned with the practice of urological surgery in one of these countries at the time of their election. There shall be the following classes:

(*a*) *Full Members* who shall be consultant urologists engaged exclusively in the practice of this speciality.
(*b*) *Associate Members* who shall be:
  (i) Consultant general surgeons devoting a large part of their time to urology;
  (ii) Junior surgeons of senior registrar grade or equivalent status, and holding a Fellowship in Surgery of one of the Royal Colleges. They should at the time of their nomination for membership be working in a department of urology under the supervision of a surgeon engaged exclusively in urology.
(*c*) *Affiliated Members* who shall be:
  (i) Appointed at the discretion of Council.
  (ii) Working/or have worked in this country at the time of their election in a urological unit for one year.

Candidates for Affiliated Membership, holding a reasonable medical qualification, may hold an Honorary appointment at registrar level.

(*4*) *Mode of Election.* (*a*) Candidates for Full Membership shall be sponsored by two *Full* Members of the Association. Their names shall be sent to the Honorary Secretary not less than six weeks before the Annual General Meeting for election. If a ballot is necessary, a majority of two-thirds of those present and voting shall be required.

(*b*) Candidates for Associate Membership shall be sponsored by one *Full* Member and one *Associate* Member, but shall be elected by the Council.

(*c*) Candidates for Affiliated Membership shall be sponsored by two *Full* Members, but shall be elected by the Council.

(6) *Subscription.* The annual subscription shall be:

Home Members: Full, £10·50; Associate, £7·50.
Overseas Members: Full and Associate, £7·50.
Affiliated Members, £6·50.

All subscriptions shall include the *British Journal of Urology*.

It was agreed to consider at the next Annual General Meeting the question of medical practitioners registered in Pakistan being eligible for membership of the Association. This would necessitate the insertion of the words "or Pakistan" after "South Africa" in Rule 3 regarding membership. It was thought that general approval should not be given to the inclusion in this Rule of any country not now in the British Commonwealth, but that each country should be considered individually on an *ad hoc* basis.

7. Election of Officers. The following were elected officers for 1972/73:

President:	Mr Howard G. Hanley
Vice-President:	Mr R. A. Mogg
Honorary Treasurer:	Mr Thomas Moore
Honorary Secretary:	Mr J. P. Williams
Honorary Editorial Secretary:	Mr W. Selby Tulloch

8. Election of Members of Council. It was reported that the following had been nominated for election to the Council:

Full Members:
Mr P. Dawson-Edwards }
Mr C. H. Kinder } by the Council
Mr K. E. D. Shuttleworth }
Mr J. Burke, nominated by Mr S. H. C. Clarke and Mr P. F. Philip.

A ballot was held and the following were elected to fill the vacancies: Mr C. H. Kinder, Mr P. Dawson-Edwards, Mr K. E. D. Shuttleworth.

9. Associate Member Representative on the Council. Mr J. N. Ward-McQuaid was elected to fill the vacancy on the Council for an Associate Member Representative.

10. Election of Auditors. Messrs Howard, Howes and Co. were re-elected auditors for the ensuing year.

11. 1973 Annual Meeting. It was reported that the 1973 Annual Meeting would be held in London from 27th-30th June. It was suggested that there should be a scientific paper session running simultaneously with films on the Friday afternoon.

12. 1974 Annual Meeting. It was reported that the 1974 Annual Meeting would be held in Torquay.

13. 1972 Provincial (One-Day) Meeting. It was reported that the 1972 Provincial (One-Day) Meeting would be held in Norwich on 14th October.

14. Chairs of Urology. It was reported that, as the result of Professor Pyrah's efforts to institute permanent Chairs of Urology throughout the British Isles, a lot of discussion had taken place on this subject during the year, both in Council and in the Standing Committee. A Sub-Committee had been set up to consider a memorandum drawn up by Professor Pyrah. This memorandum had been accepted by the Sub-Committee and approved by Council. A meeting had been held with the President of the Royal College of Surgeons of England to discuss the memorandum, which had been submitted to the University Grants Committee with copies to the President of the Royal Colleges of Surgeons in Edinburgh and Glasgow. A letter in reply had been received from the University Grants Committee giving broad approval, but pointing out that the Committee could institute Chairs on its own and that the initiative was usually taken by the universities. The President had now undertaken to write to the universities; in the first place to those where there were already Chairs of Urology, to urge them to establish permanent Chairs in the Specialty.

Professor Pyrah suggested that a deputation consisting either of the Standing Committee on the Development of the Urological Services or representatives of that Committee should be appointed to discuss this matter with the universities. Professor Swinney pointed out the enormous cost to the universities of setting up permanent Chairs and drew attention to the fact that a personal Chair was not a financial burden on the university concerned. Professor Blandy thought that Chairs of Urology would improve undergraduate teaching in urology as a number of students qualified at the present time without receiving any teaching in urology at all. A letter was received from Professor Shackman, in which he suggested that six Chairs in Urology might be established throughout the country within the next four or five years and that suitable young surgeons should make sure that they were exposed to a suitable discipline between now and the time that the Chairs were advertised as it took considerable time to complete the training as a Professor. Professor Pyrah expressed an opinion that there should be Chairs in Newcastle, Hammersmith Hospital, the London Hospital and Scotland. Mr A. Marshall thought that the post of senior lecturer should be instituted first, but Professor Blandy pointed out that if that was done there would be no appointments for these lecturers if no permanent Chairs were established.

15. Development of the Urological Services and the Training of Urologists. It was reported that two meetings of the Standing Committee on the Development of the Urological Services had been held during the year, from which the following points had emerged:

(*a*) The number of consultant posts available in 1972 had risen from 9-12.

(*b*) As a result of the questionnaire issued to members, if one equated the number of senior registrars to the number of consultant posts available between 1972 and 1974 inclusive there would be 19 senior urological registrars completing a four-year programme or 23 completing a three-year programme, and over the same period of time there would be at the present rate 20 consultant posts available.

(*c*) The members of the Standing Committee felt they had been in office too long. Professor Pyrah, Mr Hanley and Mr Poole-Wison had therefore resigned and the Committee had been re-constituted as follows: Chairman, the President, Vice-President, Immediate Past President, Honorary Secretary, Immediate Past Honorary Secretary, the Chairman of the Specialist Advisory Committee, Regional Scottish representative. The Council had agreed that the Chairman should serve for five years. It had been suggested that Mr D. Innes Williams should be elected as Chairman and he had agreed to serve in this capacity.

British Journal of Urology (1972), **44**, 617-622

URETERO-VAGINAL FISTULA[1]

D. M. WALLACE, O.B.E., M.S., F.R.C.S.

Royal Marsden Hospital and St. Peter's Hospitals and Institute of Urology

WHEN a fistula develops between the ureter (or ureters) and the vagina it may be the consequence of surgical misadventure, a stitch encircling or transfixing the ureter or a ligature applied either to include or in close proximity with the ureter. A fistula may also develop as a sequel to devitalisation of the ureter, sloughing or thrombosis, especially after irradiation or extensive surgery where the internal iliac arteries may be ligatured or resected. When an injury occurs to the ureter and this is recognised and repaired at the time of operation the outlook may be good and, in the present series, there has never been fistula formation.

Following anterior colporrhaphy or a simple abdominal hysterectomy, the ureter may be caught in a stitch and the damage not recognised at the time of operation. This is a surgical misadventure, it is not confined to the gynæcologist in training but can happen at the hands of even the most experienced surgeon. It is not generally recognised that gross dilatation of the ureters may occur in uterine prolapse—the ureteric walls are thin and may be enclosed within the prolapse (Fig. 1). The high Pacey stitch may transfix or encircle the ureter without the gynæcologist being aware that this has occurred. In 3 patients in this present series a uretero-vaginal fistula on one side only occurred after such a repair. It is probable that the fistula is a combination of trauma and obstruction, since in the days gone by vaginal uretero-lithotomy was practised without persistent fistula formation.

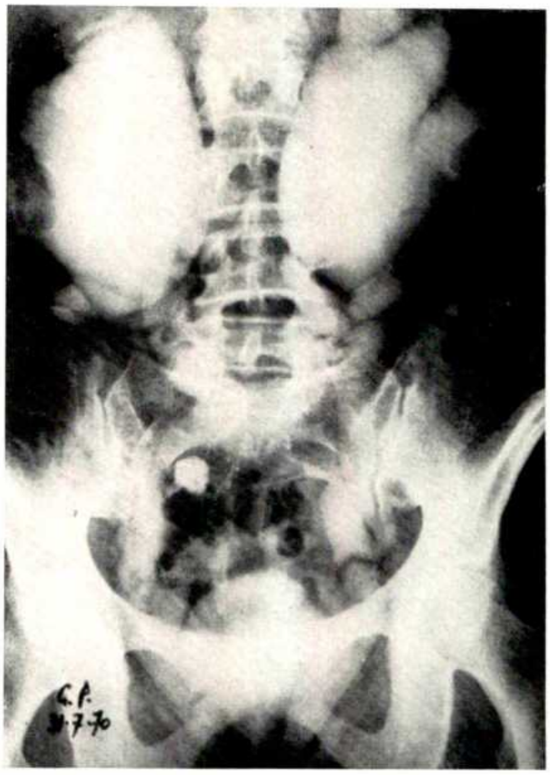

FIG. 1

Severe uterine prolapse (patient of Peter Riddle). Note dilated and elongated ureters at vaginal introitus. Complete restoration of renal function with correction of prolapse.

Abdominal hysterectomy for non-malignant conditions may result in simple fistula formation. In this type the lesion is usually low, and may well be due to the clamp applied to the uterine artery including or compressing the ureter at the lateral aspect of the cervix. In both these types of simple fistula the adjoining tissues are healthy and there has been minimal interference with the blood supply of the ureter. The complicated fistula, which predominates in this series, is the result of a combination of therapeutic methods in patients in an older age group and in the presence of malignant disease. The combination of intra-vaginal intra-uterine radium, possibly with external radiation as well, followed by radical surgery with stripping of the lateral pelvic walls and ligature of the internal iliac arteries may result in ischæmic necrosis of one or both ureters at any point below the pelvic brim. The tissues in the pelvis can no longer be considered to be normal, there may be radiation fibrosis, endarteritis or residual tumour. The surgical management of the complicated fistula and especially the bilateral fistulæ must make allowances for these factors.

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[1] Read at the Twenty-eighth Annual Meeting of the British Association of Urological Surgeons in London, July 1972.

The Simple Fistula.—In 3 patients a fistula developed after anterior colporrhaphy, an operation at which the ureter would not normally be exposed nor would many gynæcologists even be aware of its proximity or the fact that it could be elongated and dilated. The urinary leak was recognised early within 2 weeks of operation and in all there was back pressure on the kidney which settled once the fistula was fully established. Pyelography before any gynæcological operation is rare but could well warn a gynæcologist of any abnormality of the upper tract. Pyelography after a gynæcological operation in the presence of iliac fossa or renal fossa tenderness is mandatory. Occasionally a retroperitoneal extravasation may produce a paralytic ileus, in 1 patient the abdomen was reopened and even then the diagnosis was not established. Pooling of the dye on pyelography is diagnostic but may be obscured in the unilateral fistula by a distended bladder. A post-micturition film is essential if a low fistula is suspected (Figs. 2 and 3). Ureteric catheterisation was attempted in the majority of the simple fistulæ but was only successful in 2 cases—and only one of these had a normal pyelogram 6 months later. The catheter may pass through the fistula into the cavity so that if dye is injected the extravasation in the parametrium can be seen (Fig. 4). Although ureteric catherisation was unsuccessful in the majority of simple fistulæ, if the lesion is diagnosed early catheterisation may be possible. The greater number of the patients in this present series were referred from other hospitals often several weeks after the primary operation. Fistulæ may have been seen in these other hospitals but when catheterisation was successful no referral was necessary. Unless the fistula can be repaired soon after the primary operation, when the tissues are still soft, it is better to wait for at least 2 months to allow the acute reaction, hæmorrhagic extravasation and fibrosis to settle down before attempting repair. In patients referred from outside hospitals, intervention after 2 weeks is difficult, the wound œdematous and frequently infected. Intervention may be necessary at any stage if the fistula dries up with increasing loin pain and pyelographic evidence of obstruction.

TABLE I

Uretero-Vaginal Fistula

Radiation + Wertheim	18	6	bilateral
Simple hysterectomy	8	0	
Pelvic abscess	2	0	
Colporrhaphy	3	0	

The Complicated Fistula.—This was the commonest type of fistula in the present series—unilateral in 12 and bilateral fistula in 6. All these patients had intra-vaginal and intra-uterine radiation and many had supplementary external irradiation by Cobalt 60. An extended hysterectomy with node dissection and often ligature of the internal arteries had been carried out a month after completion of the radiation. Many radiotherapists believe that radiation alone will not produce obstruction to the ureter and that persistent obstruction means persistent tumour. This is incorrect. Radiation with subsequent surgery can certainly produce gross fibrosis of the peri-ureteric tissues and alteration of the blood supply to the ureter can produce necrosis. A modification of the pedicle flap fashioned in the midline and using a conjoined Wallace 1969 ureteric stoma has been used in 2 patients with bilateral obstructed ureters but where a fistula had not yet developed.

The Diagnosis of the Complicated Fistula.—Urologists and gynæcologists can learn from each other. The urologists have learnt the value of routine bimanual examinations for any pelvic

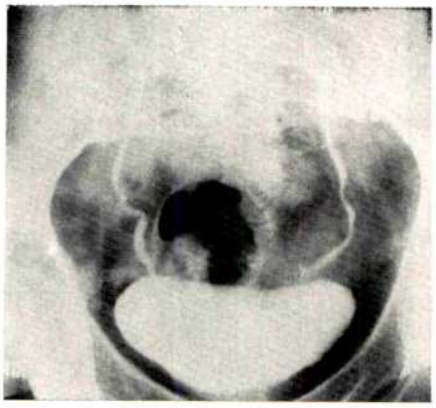

FIG. 2

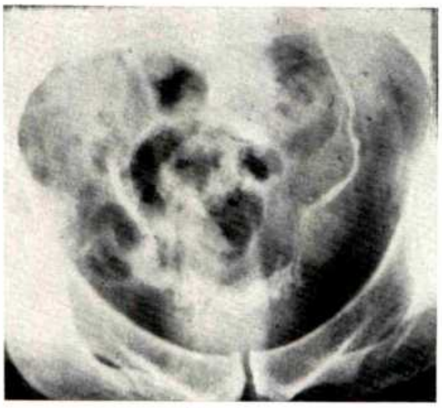

FIG. 3

Fig. 2.—Extravasation on the left largely obscured by bladder shadow.
Fig. 3.—Extravasation more easily recognised in Fig. 3 after micturition film.

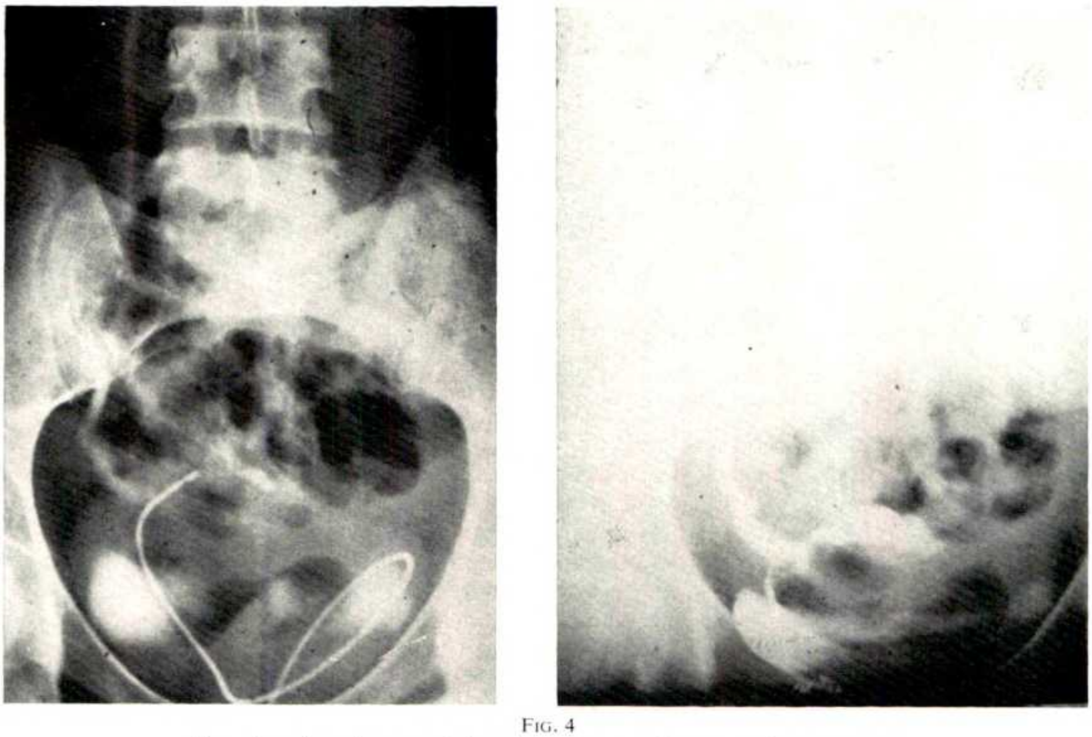

FIG. 4

Ureteric catheter has passed through the fistula and into area of extravasation.

lesion and the gynæcologists (and radiotherapists) are learning the value of pre-operative pyelography. Although dilatation of the ureters is a frequent finding after a Wertheim's hysterectomy progressive dilatation or non-function may be the earliest warning of impending fistula formation (Fig 5). Usually the patient is unwell—pyrexial with loin pain or lower abdominal guarding. Intervention, even if desirable, may not be possible. When early intervention has been attempted in a complicated fistula the tissues are hæmorrhagic and ill-defined but pedicle flap reconstruction is possible because the tissues in the true pelvis do not need to be explored.

Methods of Repair.—Reimplantation of the ureter was attempted in 4 patients. In none was the end result satisfactory. It is possible that the site of obstruction was not at the site of re-anastomosis but due to fibrosis of the lower 3-4 inches of the ureteric wall. Colpocleisis, the closing of the vaginal introitus, was used in 2 patients. The bilateral fistulæ were treated in a variety of ways. A bilateral pedicle flap left too little bladder so that in the 1 patient in whom it was attempted a nephrectomy was necessary on one side and a revision of the anastomosis on the other. An ileal loop was used but although kidney function was good where the anastomosis was isoperistaltic renal function on the other side where the flow was antiperistaltic resulted in progressive deterioration (Fig 6). The ileal loop has been used successfully where the flow is isoperistaltic in unilateral lesions where there is a considerable loss of ureteric length. Uretero-colic diversion in a case of bilateral fistula resulted in marked deterioration of renal function at 3 years.

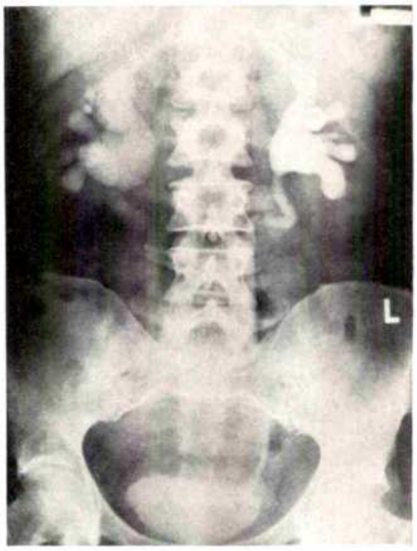

FIG. 5

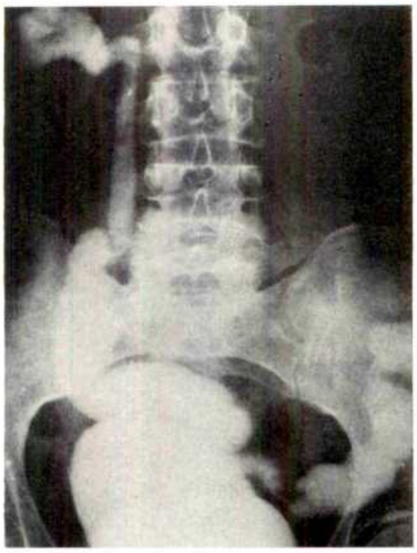

FIG. 6

Fig. 5.—48 hours before development of a fistula on the right. Previous irradiation and Wertheim's hysterectomy 3 weeks before.

Fig. 6.—Micturating cystogram in a patient with an ileal loop for bilateral fistulæ. Reflux and kidney damage on the right, no reflux on left.

The Boari Ockerblad Flap.—Although the credit is given to Boari, who in 1894 first performed this operation on dogs but never in man, the credit should be shared with Ockerblad (1947) who was the first surgeon to report the use of this method in man. Spies, Johnson and Wilson (1933) of Yale who also did experimental work on this subject, have never received any credit nor are their names mentioned in many accounts of this operation. Since it was their work that

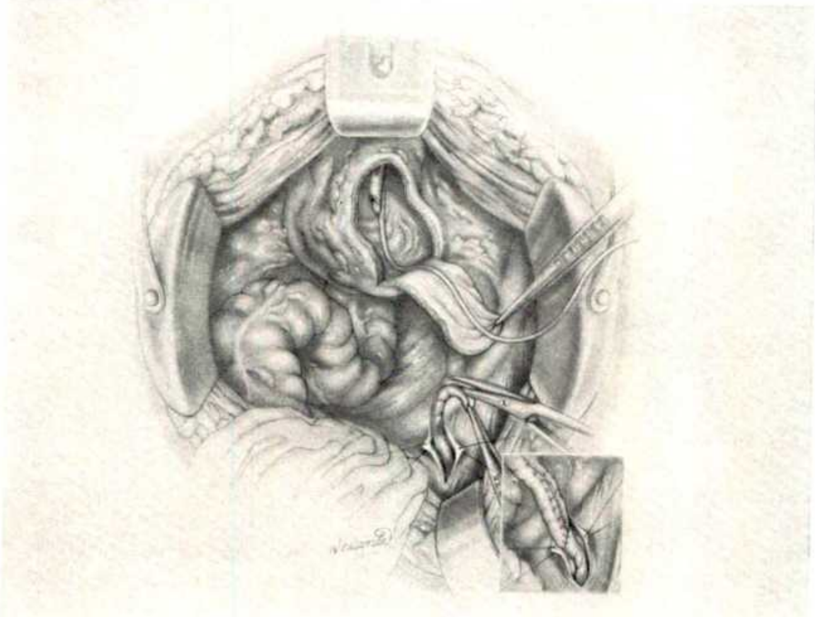

FIG. 7
Boari Ockerblad flap. Note fishtail anastomosis as a consequence of the ureter being split on posterior aspect.

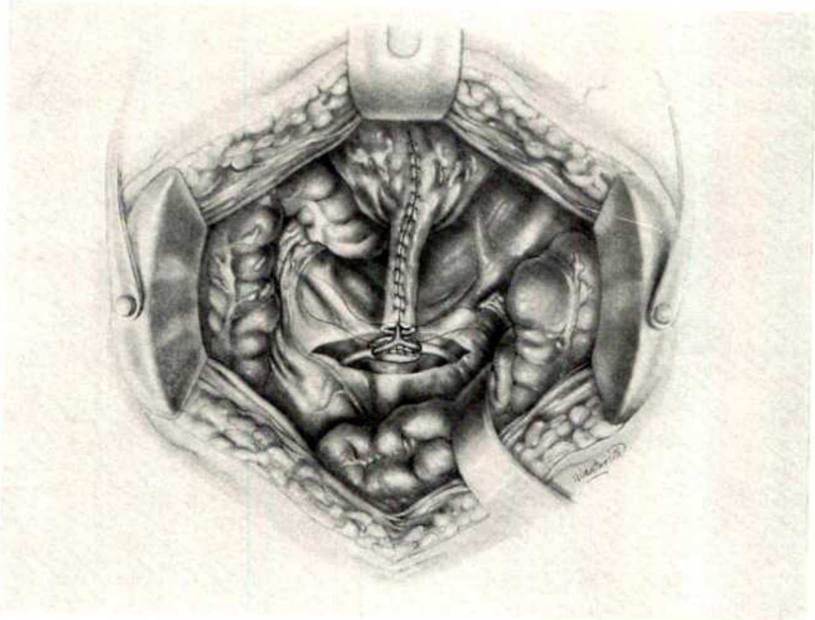

FIG. 8
Boari Ockerblad 69. A midline tube pedicle with anastomosis to a conjoined 69 ureteric stoma with drainage by Kehr's tube.

TABLE II

Uretero-Vaginal Fistula

Method	Number	Good	Results Uncertain	Bad
Colpocleisis	2	...	1	1
Reimplantation	4	...	...	4
Ileal loop	6	4	...	2
Uretero colic	3	1	...	2
Ureteric splint	2	1	...	1
Boari Ockerblad	16	12	2	2
Immediate repair	4	4	...	...

resulted in Ockerblad performing the operation in man it is fitting that they should get appropriate acknowledgement. The Boari Ockerblad flap (Fig. 7) has over the last 20 years proved its value. It is a method that can be used in the uræmic patient, it is simple to perform, and can be done either intra- or extraperitoneally. Although only 1 patient has demonstrable reflux there has been no loss of renal substance after many years in any of the patients in this series. Grant Williams and his colleagues (1971) have demonstrated that reflux in the adult, provided the urine is sterile, produces minimal kidney damage. Perhaps the most significant observation is the complete absence of post-operative complications. Where complicated or extensive fistulæ occur, and no skilled urological assistance is available, the pedicle flap, because of its simplicity, will give good results even in relatively inexperienced hands. Bilateral fistula still remains a problem although relatively rare. Fibrosis of the lower ends of the ureters is now seen more frequently, and for these patients an operation has been used that would be equally applicable to bilateral fistulæ. A midline flap is constructed based on the superior vesical arteries on both sides and going forward over the dome of the bladder to the anterior wall. In the female bladder a tube 12-15 cm. long with a base of 6 cm. can be constructed with ease. This tube is sufficiently long to reach the promontory of the sacrum. At this point both ureters are anastomosed using the Wallace 1969 technique and the tube pedicle is anastomosed to the ureteric stoma exactly as one would do with an ileal conduit (Fig 8). It is an operation that does not involve dissection in the depths of the pelvis and is effective because of its simplicity.

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British Journal of Urology (1972), **44**, 623-631

VESICAL FISTULAE INTO THE VAGINAL VAULT[1]

By John Lawson, M.B., B.Chir., F.R.C.O.G.

Newcastle University Hospitals

Vesico-vaginal fistulæ may be classified anatomically into four types, juxta-urethral, mid-vaginal, vault, and massive fistulæ in which all three are combined. Each anatomical type poses different problems which have been summarised previously (Lawson, 1968). High fistulæ may sometimes be inaccessible or even invisible per vaginam, and the lower ends of the ureters may be endangered during repair.

In my personal experience of 422 vesico-vaginal fistulæ treated since 1953, 102 were either high in the vaginal vault or in the cervix and are the subject of this paper. Eighty-five of them were treated in Nigeria, 12 in Newcastle, 2 in Uganda, 2 in Jamaica and 1 in India.

Aetiology.—Eighty-three of the fistulæ were due directly or indirectly to obstetric trauma (Table I). *Pressure necrosis* due to sloughing of the soft tissues compressed between the fœtal head and the maternal pelvis during prolonged obstructed labour was responsible for the vast majority.

Table I

AETIOLOGY OF 102 HIGH FISTULAE

Difficult delivery		
Obstructed labour : vaginal delivery	43	**83**
rupture of uterus	16	
Lower segment Caesarean section	17	
Ruptured Caesarean section scar	7	
Gynaecological operations		
Abdominal hysterectomy	15	**18**
Vaginal hysterectomy	1	
Hysterectomy + radiotherapy	2	
Direct trauma		**1**

Rupture of the uterus due to obstructed labour may involve neighbouring bladder wall already devitalised by prolonged pressure. This was a factor in 16 survivors of this dangerous obstetric complication who developed fistulæ.

Lower segment Caesarean section was responsible for 17 cases. Usually the injury occurs when the bladder is not reflected far enough downwards before the lower segment is opened. Alternatively, during the reflexion the bladder may be torn, particularly if a previous operation has made it densely adherent to the lower segment. The bladder may also be injured during Cæsarean section by the accidental passage of a suture through the posterior bladder wall during repair of the uterine incision (which can also occur during the treatment of uterine rupture). In these cases urinary incontinence is delayed until the bladder tissue caught up in the suture sloughs. In some of the vesico-uterine fistulæ which follow, monthly hæmaturia rather than urinary incontinence may be the presenting symptom.

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[1] Read at the Twenty-eighth Annual Meeting of the British Association of Urological Surgeons in London, July 1972.

Rupture of a lower segment Cæsarean section scar in a subsequent labour may also result in a urinary fistula if the tear involves the adherent bladder. Seven of my cases resulted from this chain of events.

Eighteen cases followed gynæcological operations, mostly *abdominal hysterectomy* for benign conditions (Fig. 1). These operations were usually made difficult by pelvic inflammatory disease, endometriosis, or previous surgery. However, a fistula may follow an apparently straightforward operation as a result of a small pelvic hæmatoma rupturing into the bladder during the post-operative period.

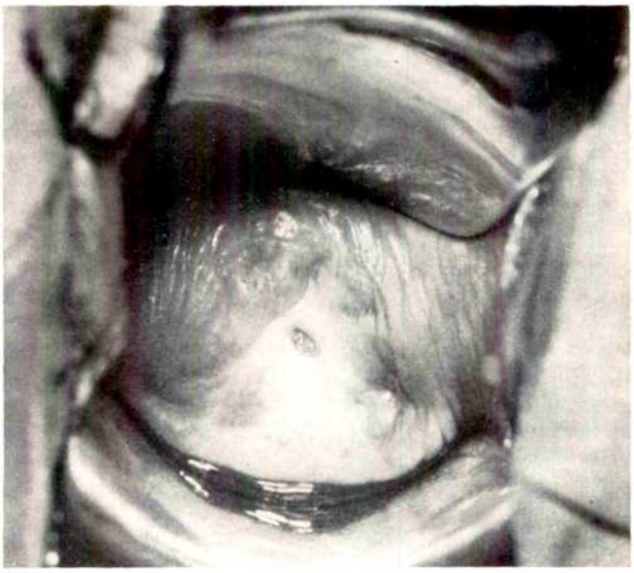


FIG. 1
Vault fistula following hysterectomy.

The danger of *radiation necrosis* of the bladder during the treatment of carcinoma of cervix is so well known that it is usually avoided nowadays. However, treatment in the modern vogue by radical hysterectomy after preliminary radiotherapy may result in surgical devitalisation of the already irradiated bladder wall, which may be sufficient to cause a fistula. It was responsible for two of those I have treated in Newcastle.

Direct injuries of the female bladder unrelated to childbirth or gynæcological operations rarely cause fistulæ. The only case in this series was a girl of 11 who fell on a stick which passed up her vagina and into the bladder just below the cervix. In parts of the world where maize is grown the sharp, 6 in. stubble occasionally produces this injury.

Complicating Factors.—*Vesical calculi* sometimes complicate vault fistulæ. In three of my cases they had to be removed before the fistulæ could be repaired. Two had formed on non-absorbable sutures (steel wire and thread, respectively) which had been left in the bladder-wall in previous repairs. In the other case, a laminated phosphate stone had followed inspissation of infected urine in a stagnant eddy in the base of the bladder below the fistula.

Urinary infection is, surprisingly enough, not a prominent pre-operative complication except when there have been previous attempts at repair followed by indwelling catheter drainage: in these cases a *Pseudomonas pyocyanea* infection is frequently present and is difficult to eradicate.

Previous attempts at repair certainly prejudice the result. Each operation provokes the formation of more scar tissue and diminishes the blood supply: the law of diminishing returns operates, as the prospects for successful closure recede with each successive operation. Sixteen of the 102 cases presented had had previous attempts at repair before they came into my hands, 3 of them more than once.

Initial Management.—Time is a great healer and a proportion of the smaller fistulæ will heal spontaneously. This may be assisted in the early stages by continuous catheter drainage, which is always worth persevering with for several weeks after the causative trauma, provided the patient is kept dry by the catheter. Low-pressure suction may be necessary. I have not observed spontaneous healing after a longer interval than 10 weeks after the original injury.

Since all fistulæ heal-in spontaneously to some extent even if they do not close completely, no repair should be attempted until at least 3 months have elapsed since the causative trauma, to take advantage of this. This interval also allows infection to subside, sloughs to separate and tissue planes to be re-established. For the same reason a further attempt at repair after an unsuccessful operation should be deferred for at least two months.

Where radiotherapy has been a contributory factor a much longer interval may be required, while the progressive obliterative endarteritis subsides. Attempts at repair should therefore be deferred in these cases until sloughing ceases and the tissues are quiescent, which may be up to a year.

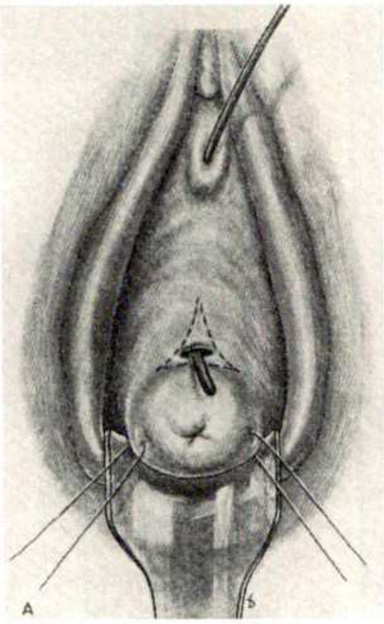


FIG. 2

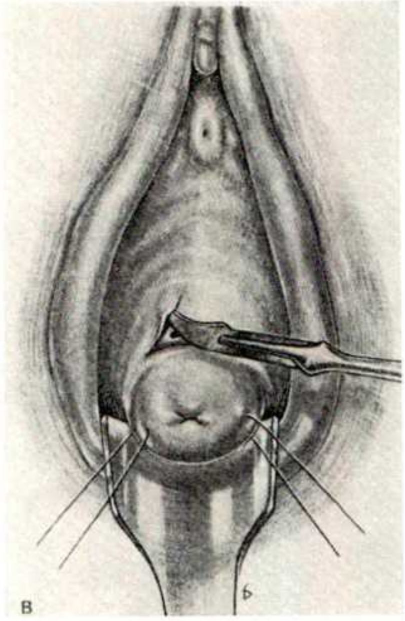


FIG. 3

Fig. 2.—Fistula in anterior fornix following obstructed labour.
Fig. 3.—Triangular incision in vaginal wall with wide base towards the cervix.

Surgical Treatment.—As in all fistula work versatility is essential. Gynæcologists traditionally prefer the vaginal approach (Moir, 1967) and urologists the abdominal approach: one of the purposes of this paper is to show that there is a well-defined place for each route.

The decision depends on accessibility, which is decided at preliminary examination under anæsthesia. If the fistula can be easily reached per vaginam, repair by this route is preferred as the post-operative period is much more comfortable for the patient than after abdominal repair

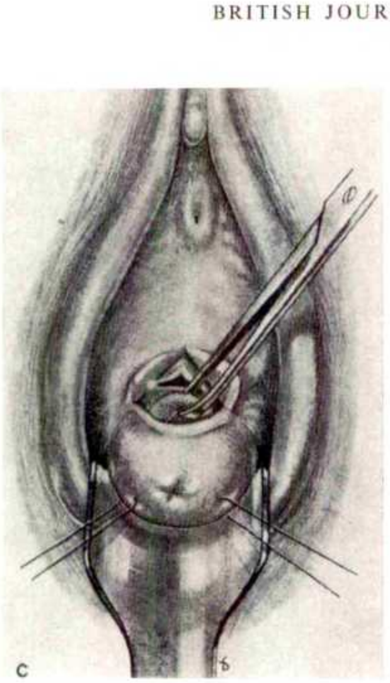


FIG. 4

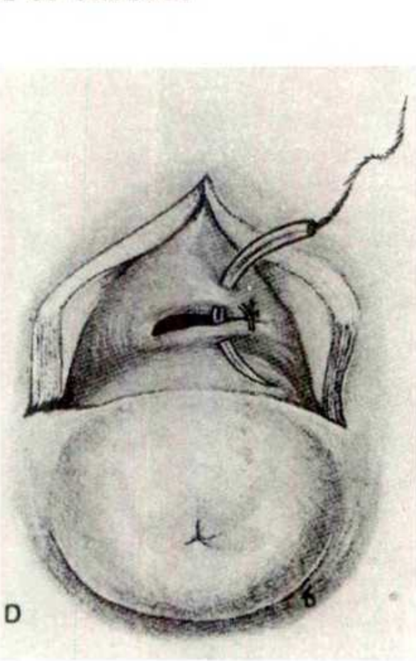


FIG. 5

Fig. 4.—Vaginal edges are freed and underlying bladder is mobilised from cervix by swab dissection.

Fig. 5.—The first row of sutures is placed horizontally in the bladder wall inverting the edges of the fistula towards the lumen.

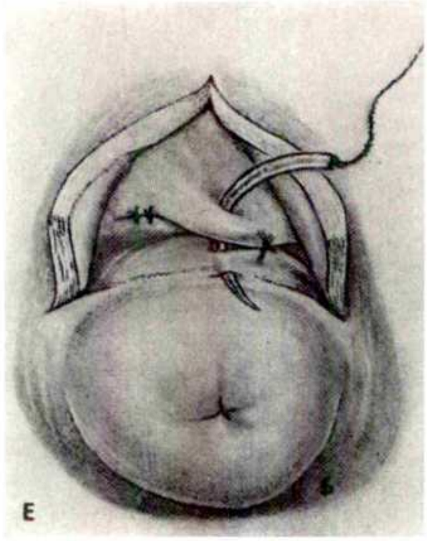


FIG. 6

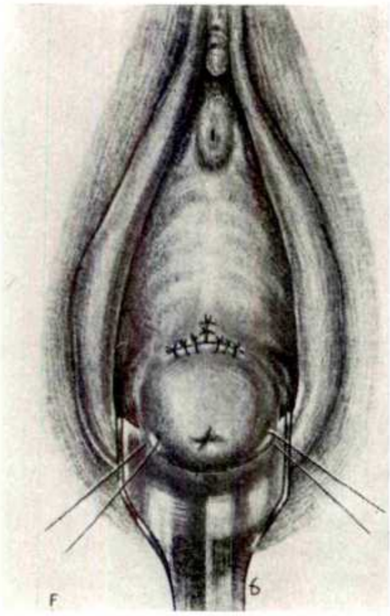


FIG. 7

Fig. 6.—The second layer of the bladder repair rolls the first layer against the intact cervix.

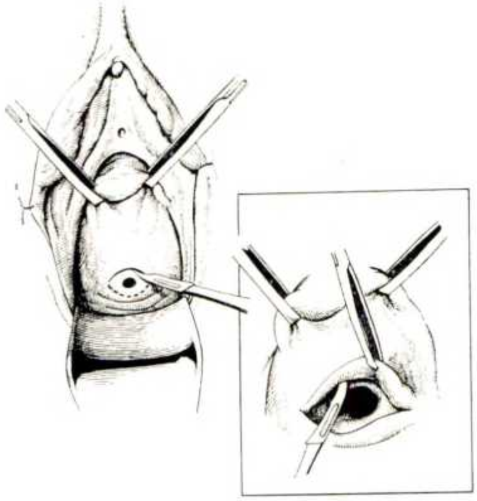
Fig. 7.—Repair of the vaginal wall, converting the triangular incision into an inverted T.

and there is less blood loss. However, when the fistula is tethered high in the pelvis and cannot therefore be made accessible by pulling down the cervix or vault, the abdominal approach is best.

The techniques used by the author have been described in detail elsewhere (Lawson, 1967) and are summarised below.

Vaginal Repair Techniques.—When the cervix is still present, this is drawn down and the bladder is dissected off it before repairing the defect in layers (Figs. 2-7).

After hysterectomy, vault fistulæ which are approachable per vaginam can be dissected and repaired in layers (Figs. 8-10).



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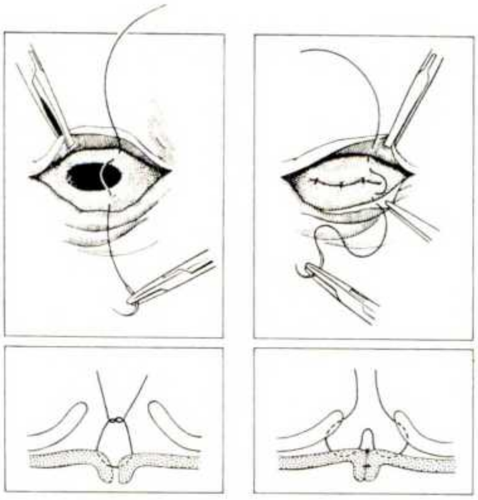

FIG. 9

Fig. 8.—Elliptical incision in vaginal vault round fistula, with mobilisation of underlying bladder.

Fig. 9.—Closure of bladder defect transversely with two layers of interrupted catgut sutures.

Fig. 10.—Closure of vaginal incision transversely, drawing intact vaginal wall over bladder repair.

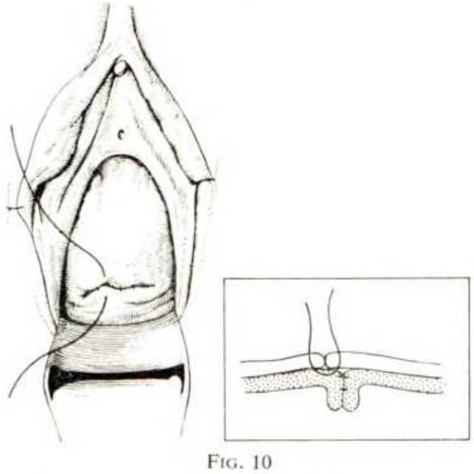

FIG. 10

Saucerisation is the alternative: high colpocleisis, which makes use of this technique, is best for radiotherapy fistulæ where the tissue planes are obliterated and the fistula is solidly fixed in scar tissue.

Abdominal Repair Techniques.—If there is still a uterus the intravesical route is preferred (Figs. 11-15). This avoids intraperitoneal dissection between the bladder and cervix which may

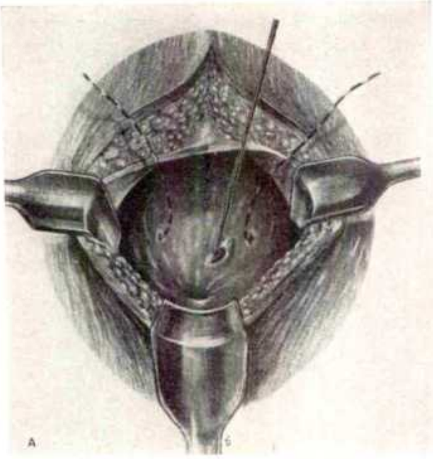

FIG. 11

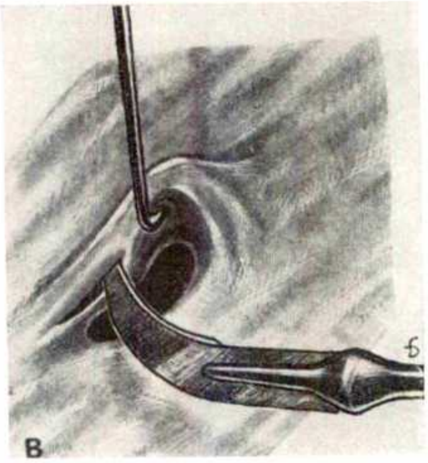

FIG. 12

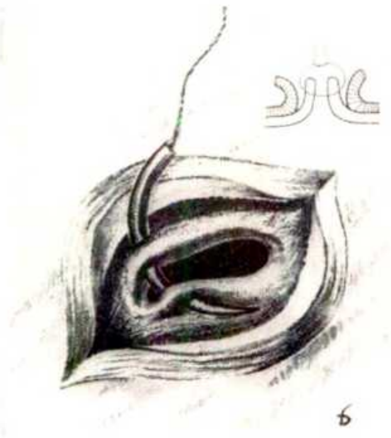

FIG. 13

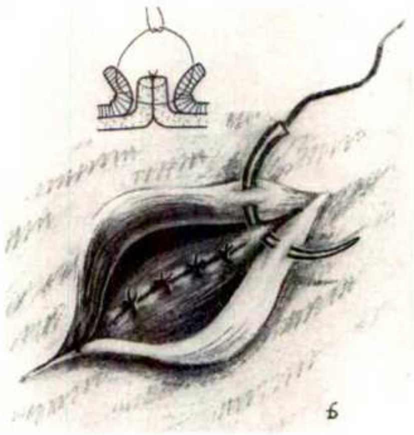

FIG. 14

Fig. 11.—Fistula exposed for intravesical repair. Catheters have been passed up the ureters as markers.

Fig. 12.—Steadying the fistula with an angled sharp hook, the bladder wall is dissected off the underlying cervix or vagina.

Fig. 13.—Defect in the cervix or vagina is repaired with interrupted catgut sutures.

Fig. 14.—The main strength of the repair is in a row of interrupted sutures in the bladder wall. Dead spaces are obliterated by including the underlying tissues.

Fig. 15.—The epithelial margins of the fistula are approximated by a continuous catgut suture which prevents intravesical bleeding from the cut edges.

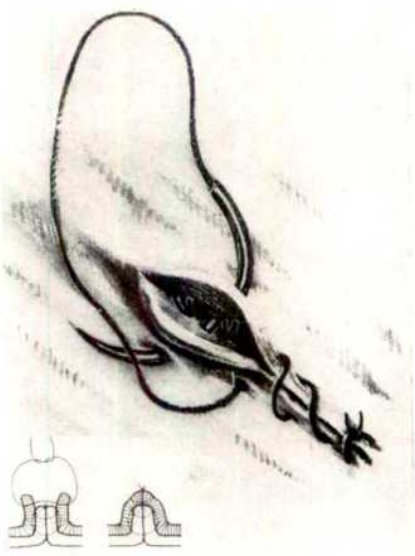

FIG. 15

be made difficult by dense adhesions. A particular advantage of intravesical repair is that ureteric catheters can be passed under direct vision as a preliminary, and the ureteric orifices thereby avoided.

When the uterus has already been removed an alternative abdominal method is transperitoneal, splitting the fundus of the bladder in the midline down into the fistula. This is particularly suitable for post-hysterectomy fistulæ inaccessible from below, as it gives good access.

In the series of 102 cases presented, one-third were approached per abdomen and two-thirds per vaginam (Table II).

TABLE II

TREATMENT OF 102 HIGH FISTULAE

Repair per vaginam		
In layers	60	**65**
Saucerisation	5	
Repair per abdomen		
Intravesical	30	**37**
Transperitoneal	7	

After-treatment.—Continuous drainage of the bladder for at least 10 days after surgical repair is essential to protect the suture line and allow firm healing.

After vaginal repairs continuous drainage per urethram into a sterile bag with a non-return valve is preferred. The amount of urine collected is noted every hour to detect blockage of the catheter without delay.

After abdominal repairs the bladder is drained through a large mushroom catheter suprapubically, as well as through a urethral catheter. The object of the double drainage is to facilitate irrigation of the bladder during the first few post-operative days until the urine clears, clot retention being much more common after intravesical repairs than after repairs by the vaginal route. After the fourth day the suprapubic catheter is removed and urethral drainage is continued for the next 10 days, during which the suprapubic cystostomy will close.

Post-operative Complications.—As would be expected the main post-operative complications of high fistula repairs are hæmorrhage, interference with the lower ends of the ureters and breakdown of the repair.

Post-operative hæmorrhage into the bladder may lead to clot retention, and extravesical hæmorrhage may lead to retropubic hæmatomas.

It is easy to include the lower end of a ureter in the repair of a high fistula. In intravesical operations ureteric catheters are efficient markers to prevent this. In one case it was necessary to begin by dividing a ureter and reimplanting it higher in the bladder before closing the fistula, and in another both had to be dealt with in this way.

One must be particularly aware of the danger to the lower end of the ureters during repairs by the vaginal route. Ureteric obstruction or misdirection leading to extravasation should be watched for post-operatively, and in two of my cases subsequent reimplantation was necessary.

After a repair operation persistent vaginal leakage of urine unstained by dye instilled into the bladder may reveal a pre-existing ureteric fistula into the vaginal wall lateral to the edge of the fistula. These had to be dealt with later in two cases in this series.

Lastly, breakdown of the repair may occur. This may be due to infection, secondary hæmorrhage, interference with free post-operative catheter drainage (usually due to poor nursing care), or—most commonly—imperfect surgical technique.

RESULTS

In this series of 102 high fistulæ, 86 were successfully closed at the first attempt (Table III). The proportion of failures in the group repaired per vaginam was one-sixth, the same as the proportion of abdominal repair failures. All the patients were ultimately cured except two: one of them stubbornly refused further treatment and the other died of intercurrent disease before a second attempt could be made to close her residual fistula.

Table III

RESULTS OF TREATMENT OF HIGH FISTULAE

	Total	Success at first attempt
Vaginal repair	65	55
Abdominal repair	37	31
	102	**86**

On review, it appears that three of the unsuccessful cases initially approached per vaginam would have been better repaired per abdomen by the intravesical route. One of the abdominal repairs, my first radiotherapy fistula, would certainly have been better done by the vaginal route: the second attempt, by high colpocleisis, was surprisingly easy.

CONCLUSION

In a series such as this, of mainly obstetric fistulæ treated in developing countries, it may be difficult to achieve the ideal of closing all fistulæ at the first attempt. However, the best results are obtained by choosing from a variety of available techniques the one which suits the individual case.

SUMMARY

One hundred and two of 422 vesical fistulæ personally treated since 1953 were either high in the vaginal vault or in the cervix. The majority were due to pressure necrosis during obstructed labour: 24 followed lower segment Cæsarean section, 16 followed hysterectomy and 2 resulted from the combined effects of surgery and radiotherapy.

The repair techniques used by the author are summarised. Most of the fistulæ were approached per vaginam, but in 37 cases the fistula was fixed high in the pelvis and abdominal repair was therefore preferred, usually by the intravesical route. Four uretero-vaginal fistulæ had to be dealt with subsequently.

Eighty-six fistulæ were successfully closed at the first attempt and the remaining 16 patients were all cured later except 2, who were lost to follow-up.

I am grateful to Mr D. Simmonds of Ibadan for Figures 2-7 and 11-16, and to Mr D. Hammersley of Newcastle upon Tyne for Figures 8-10.

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FISTULAE INVOLVING THE ADULT MALE URETHRA[1]

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The London and St. Peter's Hospitals

CONGENITAL fistulæ between urethra, perineum and rectum present important and complex problems to the pædiatric urologist, and urethrovaginal fistulæ following the trauma of childbirth constitute a whole field of specialised surgery on their own, nevertheless we intend to ignore both of these types of urethral fistulæ, and concern ourselves with the problems posed by urethral fistulæ in adult males. In Britain today such fistulæ are perhaps not common but, with the increasing severity of traffic injuries, we are likely to see more of them; and we cannot ignore the existence of what is arguably the commonest urological condition in a large part of Africa—the complicated urethral stricture, of which fistula is an important part (Singh, 1967). We thought it might be useful to survey our recent experience in order to see whether any useful lessons had been learned from these cases.

The Series

Between 1964 and 1971, 41 urethral fistulæ have been indexed in the authors' cases. Sixteen of these were temporary post-operative urine leaks following straightforward operations on the urethra, usually for stricture or hypospadias, and they closed on their own. They are of no interest except insofar as they illustrate the general principle that a fistula will close spontaneously provided there is no distal obstruction and no foreign body. Most of them involved the shaft of the penis.

TABLE I

Urethral Fistulæ in Adult Males

Temporary		Following urethroplasty and other operations on the urethra	16
Chronic	1	Post-operative fistulae	
		(*a*) After urethral operations	7
		(*b*) After prostatectomy	3
	2	Inflammatory	6
	3	Traumatic	8
	4	Trophic	1
		Total	41 cases

It is obviously the chronic fistulæ which form the main difficulty. Of these the largest single group were those which were caused by the surgeon. We had to operate to close 6 fistulæ which persisted after operations on the urethra. As a rule these were small skin-lined fistulæ which followed urethroplasty: if in the shaft of the penis they were simply freed up and oversewn, and the skin was closed over them with a suitable dorsal relaxing incision. If in the bulbar part of the urethra they were usually related to an over-large skin pocket formed in the second stage of the urethroplasty, and to close them it was necessary to trim away the surplus skin of the pocket. One unusual problem sometimes presents itself, namely a large defect in the anterior urethra following an old previous stricture operation or hypospadias repair. It may help (Fig. 1) to reinforce the closure of this fistula by rotating a flap of skin from the scrotum.

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[1] Read at the Twenty-eighth Annual Meeting of the British Association of Urological Surgeons in London, July 1972.

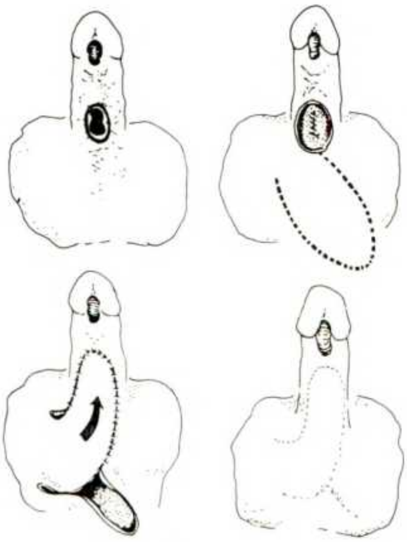


FIG. 1

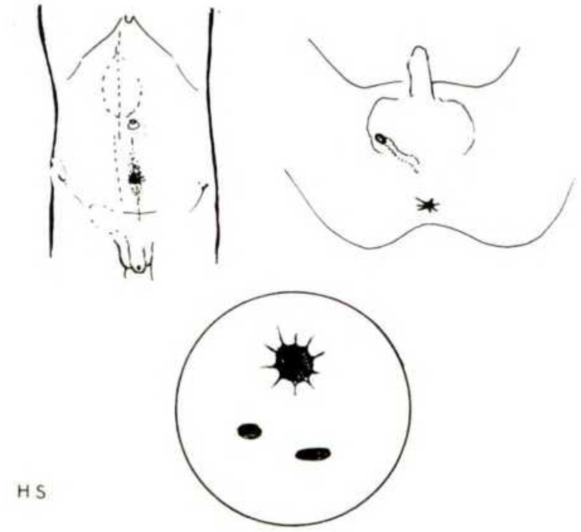


FIG. 2

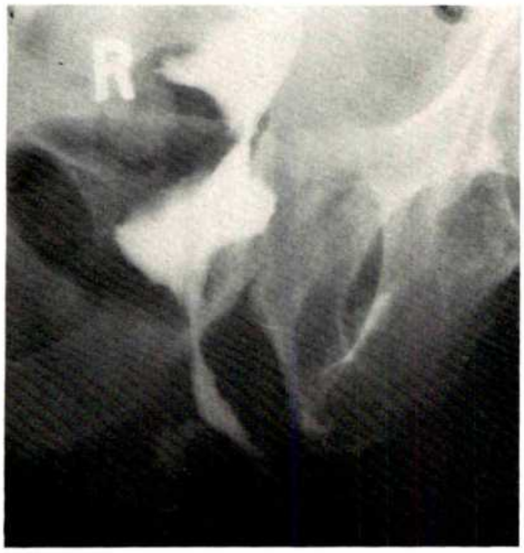


FIG. 3

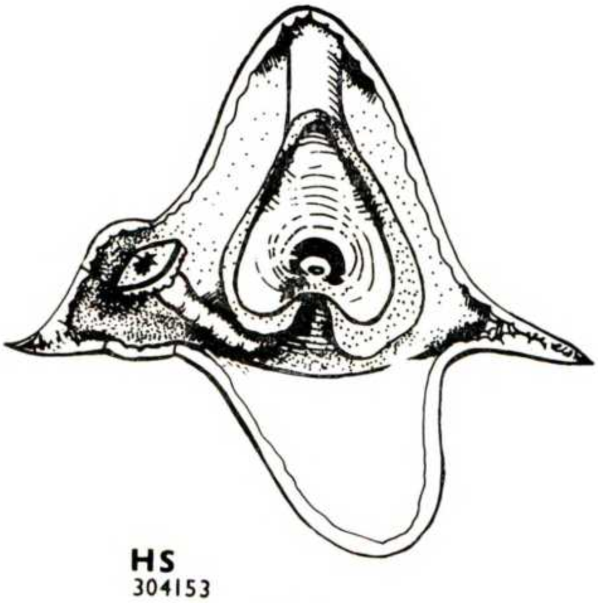


FIG. 4

Fig. 1.—A large skin-lined fistula on the ventral surface of the shaft of the penis may be closed with the help of a rotation flap of scrotal skin.

Fig. 2.—Four years after a form of prostatectomy this patient had a urethral stricture, a scrotal fistula with two internal openings, a persistent suprapubic fistula, and total incontinence.

Fig. 3.—A urethrogram showing the fistula in the bulbar urethra.

Fig. 4.—At operation the fistula was dissected back to its internal communication near the bulb and the stricture was corrected with a scrotal flap.

Two of the post-operative fistulæ followed retropubic prostatectomies done elsewhere for small fibrous prostates. They occurred early in the series, before Kilpatrick and York Mason (1969) had described their elegant method of closing these fistulæ, and they were tackled by a modification of the scrotal-flap urethroplasty at which the prostatic urethra was approached from below and the abdomen was opened from above. After dissecting the urethra away from the rectum a plug of omentum was interposed, and then over and on top of this was sutured the flap of scrotal skin. When this had healed a second stage urethroplasty was performed in the usual way (Blandy *et al*, 1968, 1971). These cases, if seen today, would have been treated along the lines laid down by Kilpatrick and York Mason and would have been spared two much more traumatic operations.

The third fistula which followed prostectomy was of a different kind altogether:

H. S. aged 83 (L. H. No. 304153), a retired surgical appliance maker. He had undergone a transvesical prostatectomy elsewhere 4 years previously. It had left him incontinent, and in addition he had a long posterior urethral stricture, a discharging suprapubic fistula, and a periurethral phlegmon from which emerged a fistula communicating with the urethra. The combination of three incontinent urinary openings was too much even for his skill as an appliance maker. The fistula was excised (Figs. 2-4) and traced up to the hole in the posterior urethra. The stricture was enlarged with a scrotal flap urethroplasty which was closed 3 months later. His suprapubic fistula closed and he not only healed his fistulæ, but became continent of urine, the explanation for which is still wanting.

Inflammatory Strictures (6 cases).—Although none of our cases have had quite the florid features of the watering-can perineum of the tropical fistulæ (Singh, 1967), nevertheless they had some unusual presentations and gave rise to some difficulties in management:

F. H. aged 50 (St P. 53821). When he was 25 he had an episode of dysuria and urinary infection. He was told he had a "congenital urethral stricture" and was treated by a brief course of urethral dilatations and was then told he was cured. And so he seemed to be for a further 15 years, until he began to get recurrent episodes of painful swelling of the right side of the scrotum, which eventually began discharging fluid, sometimes pus and sometimes urine. Examination revealed (Figs. 5-6) a sinus opening near the right testicle, which could be felt to run back towards the urethra. A urethrogram showed a stricture and a short false passage, but the sinogram failed to show a communication with the urethra. At the scrotal-flap urethroplasty the sinus was found to track right back towards the bulbar urethra and disappear in an abscess just to the right of the bulb itself, perhaps in a Cowper's gland. Section of the tissue only showed granulation tissue and no evidence of tuberculosis. Shortly afterwards he underwent the second stage of the urethroplasty without complication.

Not only may the external opening of the fistula give rise to a difficulty in diagnosis, but the periurethral abscess may be of an alarming size.

C. R. aged 30 (L.H. 34110.55). This man was subjected to a left nephrectomy at the age of 15 for a hydronephrosis. When he was 22 he sustained a trivial injury to his scrotum. This was followed by an abscess which was aspirated, and from that day onwards he suffered a succession of illnesses in which urinary obstruction due to a urethral stricture (Fig. 7) was complicated by periurethral abscesses and recurrent urethral fistulæ. Eventually he reached the state that whenever his catheter was removed he developed another abscess and another fistula. Finally he was admitted with an enormous periurethral abscess which communicated not only with the left side of the bladder—or perhaps the left ureteric stump—but also with the right ischiorectal fossa (Fig. 8). A suprapubic drain was inserted as the first procedure. A few months later when the perineal area was a little more healthy a laterally based inlay of scrotal skin was placed into the urethral stricture, and 6 months later the urethroplasty was closed. Since then he has remained well and free from symptoms.

Not every urethral fistula which accompanies a periurethral abscess is the result of an associated stricture. One was due to tuberculosis, and is described in detail elsewhere (Symes and Blandy, 1972). Here a narrow fistula between a cavitated tuberculous prostate communicated with the rectum and with a periurethral abscess. With suprapubic drainage, antituberculous chemotherapy, and finally the removal of a small calculus from the fistula it healed up spontaneously.

True "watering-can perineum" was also seen in a second case of tuberculosis (Symes and Blandy, 1972), and on this occasion the presence of a stricture necessitated urethroplasty in

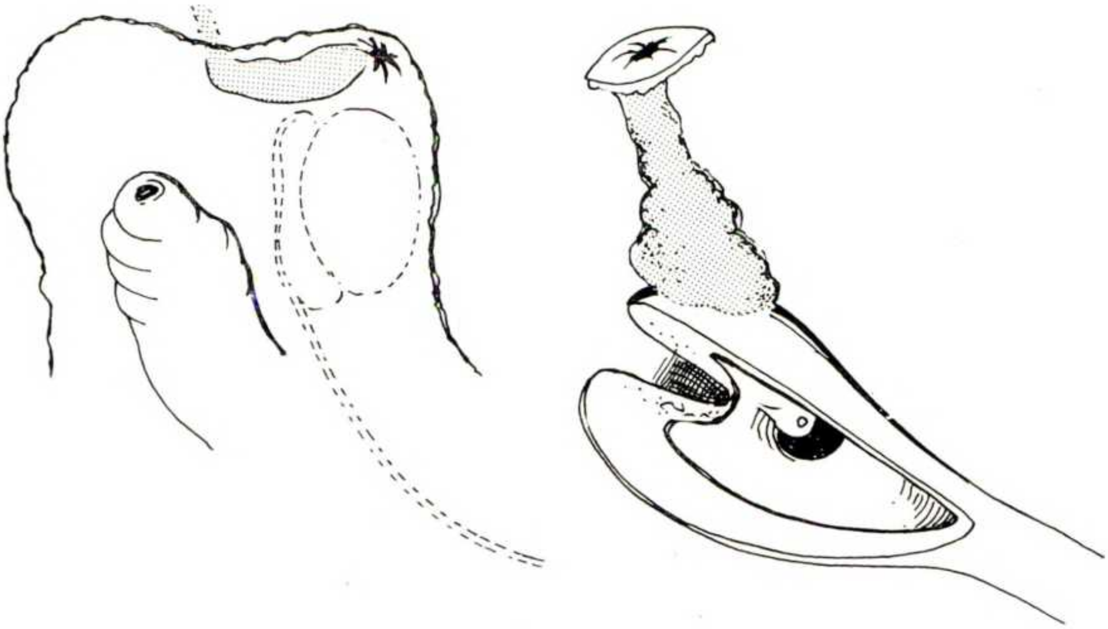


FIG. 5
This fistula opened on the skin of the scrotum and mimicked an epididymal sinus.

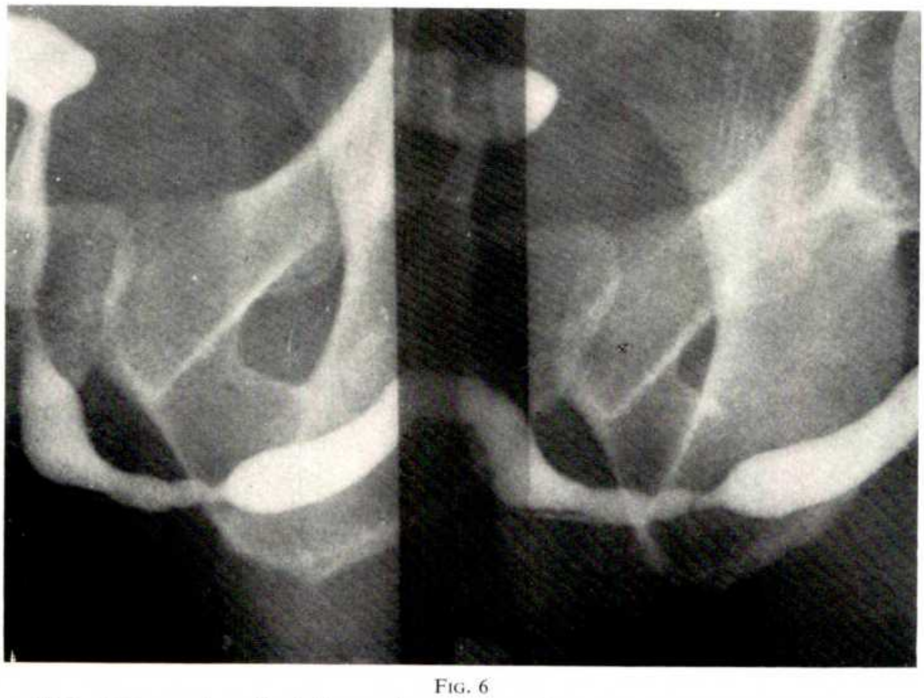


FIG. 6
The urethrogram shows the stricture and a short channel near the (presumed) internal opening of the fistula.

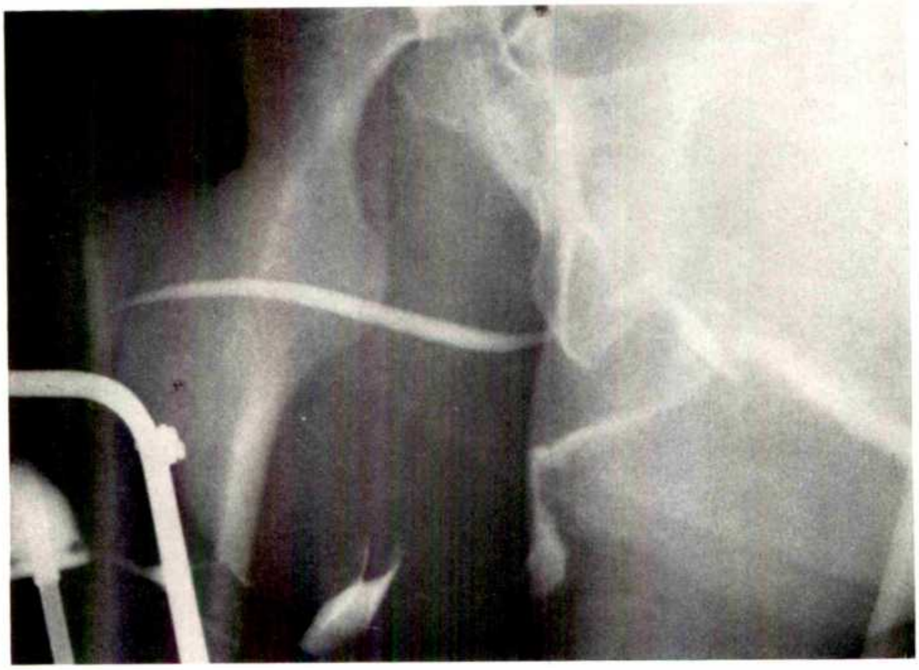


FIG. 7

The urethrogram shows the fistula tracking up to the region of the bulb.

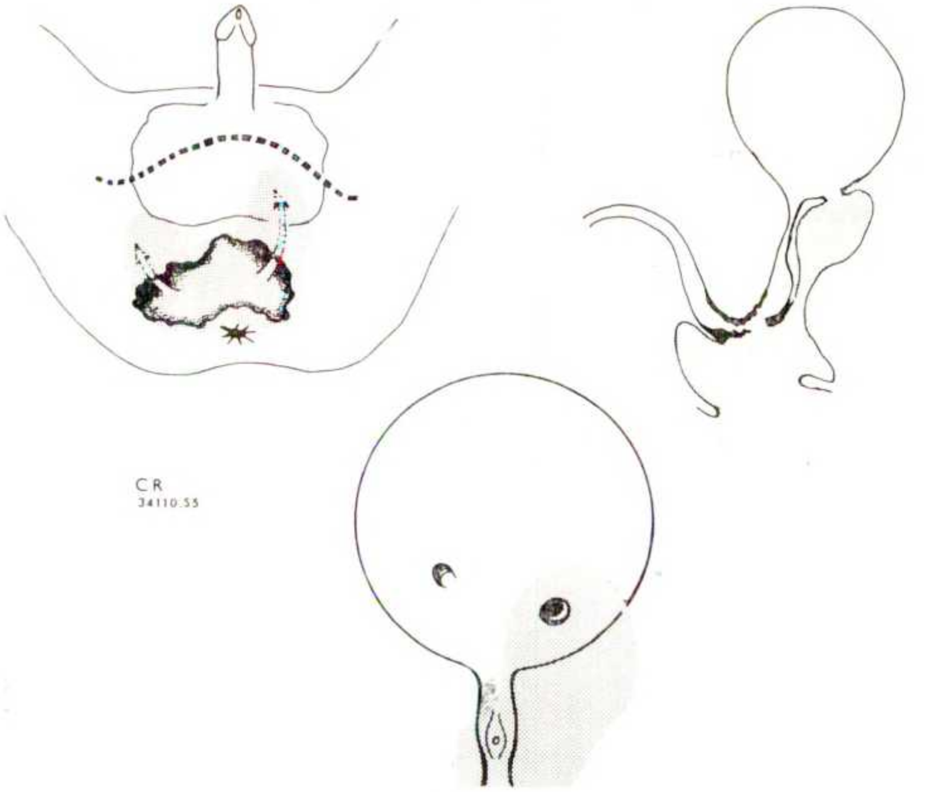


FIG. 8

The para-urethral fistula extended right up to the level of the trigone and communicated with the bladder.

addition to chemotherapy for the underlying disease. The same multiple perineal urethral fistulæ were also a feature of an unusual case who had a pulmonary infection due to *Mycobacterium kansassii* and every appearance in the perineum of a tuberculous infection there too, though no mycobacteria could be cultured from its secretions (Symes and Blandy, 1972).

Traumatic Fistulae: (8 cases).—Today many strictures are seen as a result of injury to the pelvis and laceration or disruption of the prostatic urethra. Few of them end up with a fistula.

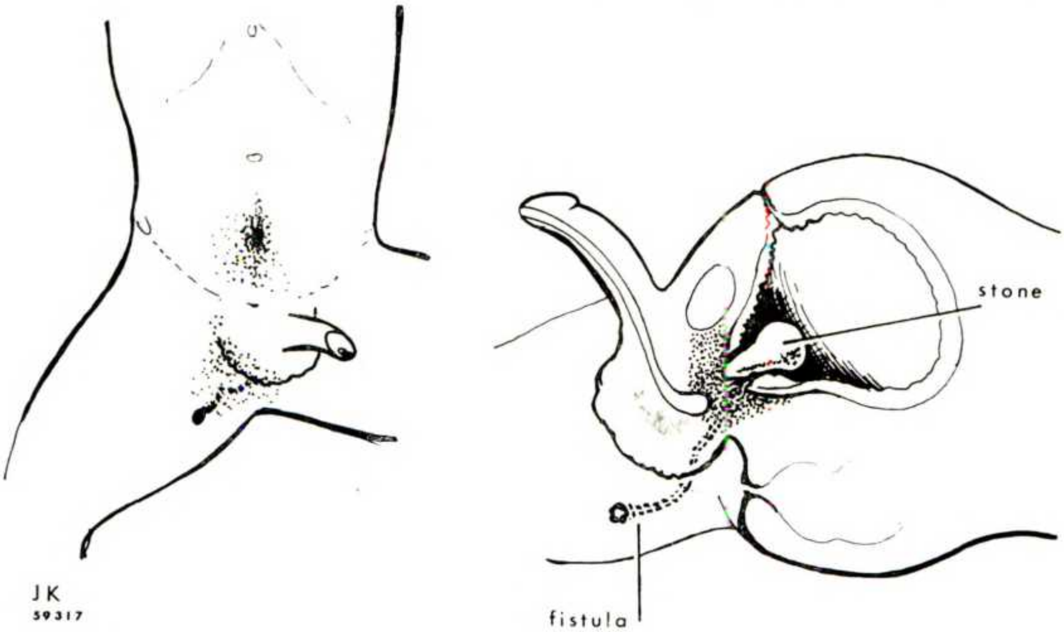


FIG. 9

Eight years after his urethral injury this patient had fistulæ opening on the abdominal wall as well as on the right thigh, and a calculus in the prostatic fossa.

One of our cases had a long and complicated stricture, for which a previous pull-through urethroplasty had been performed, but which still left him with a fistulous track which ran down to the thigh. This would open and discharge whenever the urethral stricture became stenosed again (and it needed occasional dilatation). Careful instrumentation of the urethra combined with removal of several vesical diverticula has rendered the patient symptom-free and his fistula has remained healed.

Strictures which follow pelvic fractures are commonplace, and do well with urethroplasty. But in this series we have met with three separate problems associated with very severe injuries of the pelvis, which in turn lead to strictures and fistulæ.

The first of these problems can be summarised as the "impossible gap". Here, as a consequence of the fracture, there is a long gap between one blind end of the urethra and the dislocated prostatic urethra. How to bridge the gap is the problem. It is illustrated by the following case history:

J. K., aged 31 (St P. 59317). This patient was crushed by a tractor in December 1963. He sustained a severe injury to his pelvis and a torn urethra. With intensive initial treatment he survived, leaving him with a stiff right hip, a urethral stricture which was virtually impossible to instrument, and a fistula leading from the prostatic urethra to his right thigh. To help with keeping the urethra open, a prostatectomy was performed in 1968, but when he was transferred to St Peter's in 1971 he had a narrow fistula in the suprapubic region, a calculus occupying his prostatic cavity, a fistula tracking down his thigh, and a long gap between the prostatic urethra and the stump of the bulbar urethra (Figs. 9-11). We began with a scrotal flap approach, but on following the urethral lumen, it disappeared into solid, dense, almost impenetrable scar tissue. The bladder was thereupon opened, and a bougie driven down from above (after removing the calculus). When a way had been cut through the scar tissue, the scrotal flap was formed into an inside-out tube, stitched to a silicone rubber catheter, and drawn up to lie at the bladder neck. There it remained for 3 weeks, when the tube fell out. Six months later the second stage of the urethroplasty was completed uneventfully. To our surprise the patient is completely continent (Figs. 12-15).

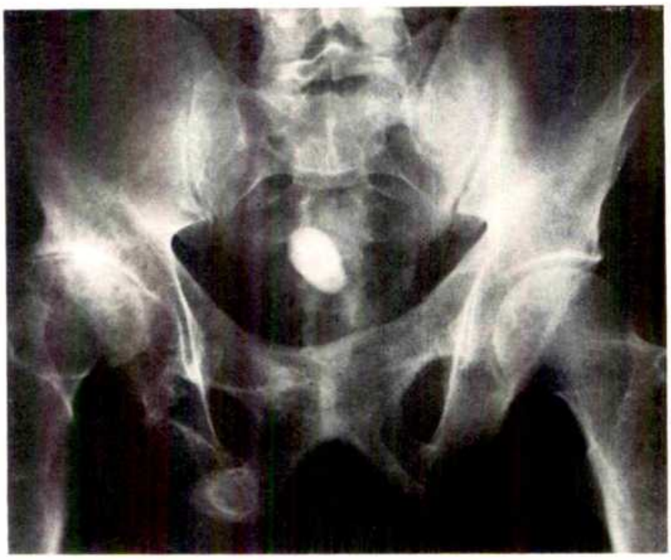


FIG. 10

The plain radiograph shows the stone in the bladder and the deformed pelvis.

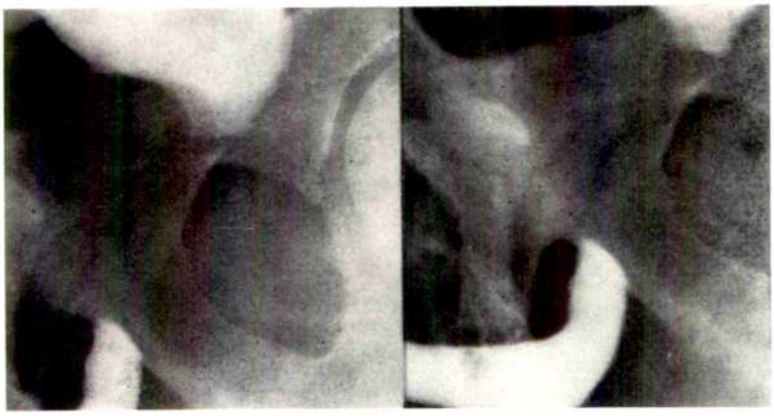


FIG. 11

The cystogram and urethrogram show the long gap between urethra and bladder base.

The second of these problems can be described as the "impossible block". In this patient, who was run over by a tractor, the pelvis was crushed, the rectum lacerated, and the urethra torn across. Only the most skilled and determined intensive therapy saved his life. He was eventually transferred to St Peter's Hospital with a transverse colostomy and a suprapubic

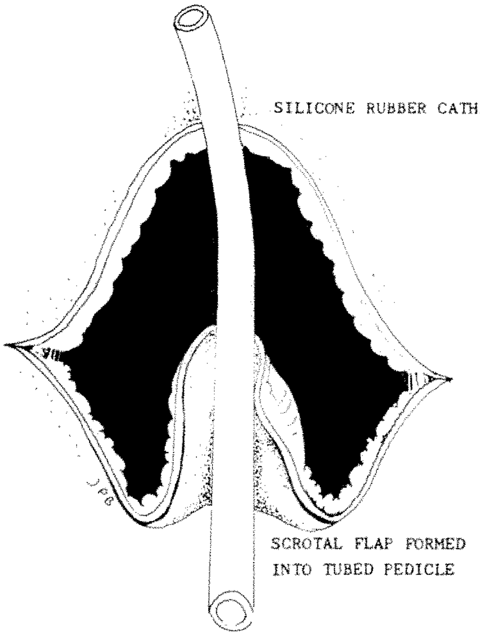


FIG. 12

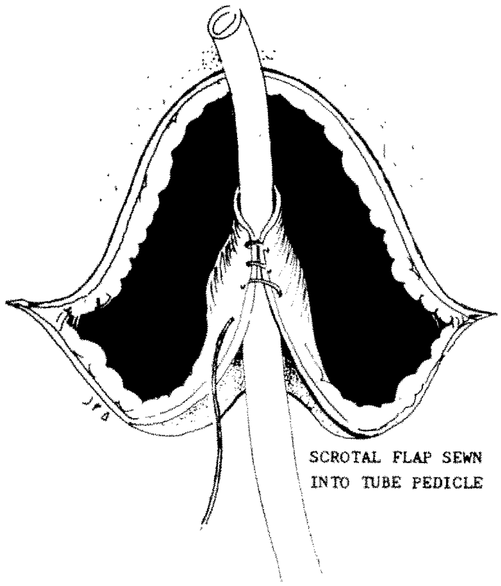


FIG. 13

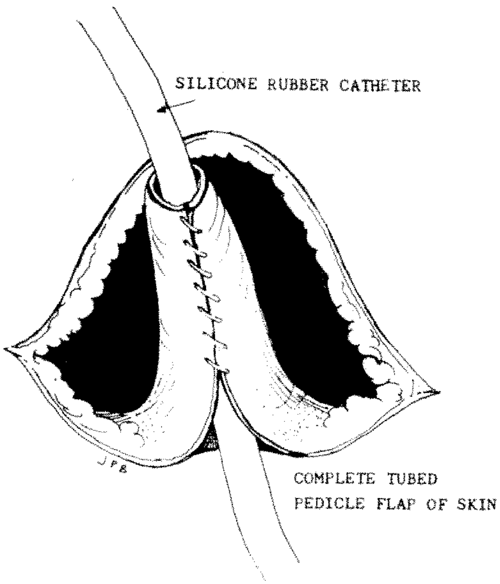


FIG. 14

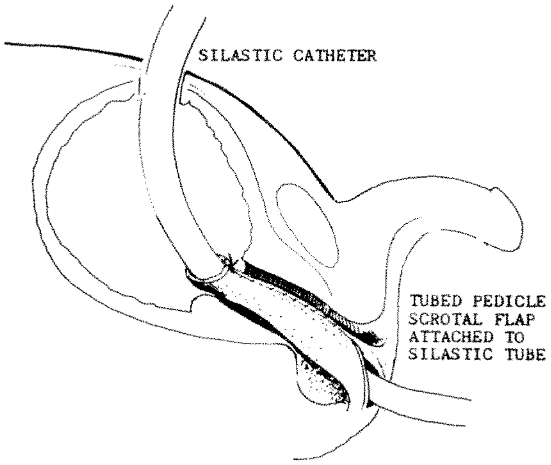
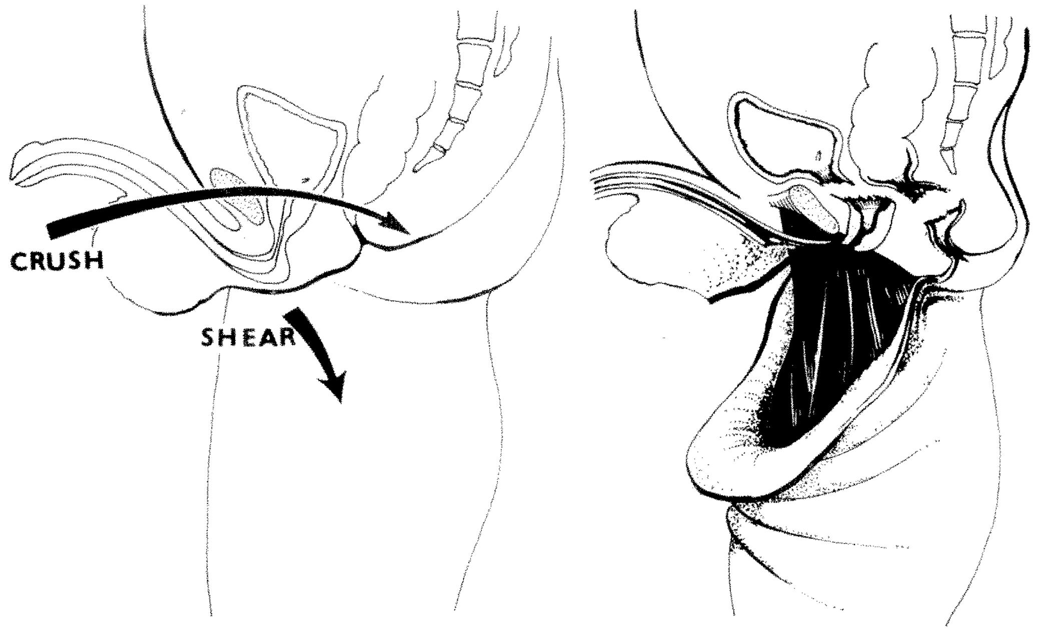


FIG. 15

FIGS. 12-15

The scrotal flap was formed into a long tube, attached to a length of Silastic tubing and drawn up into the bladder.



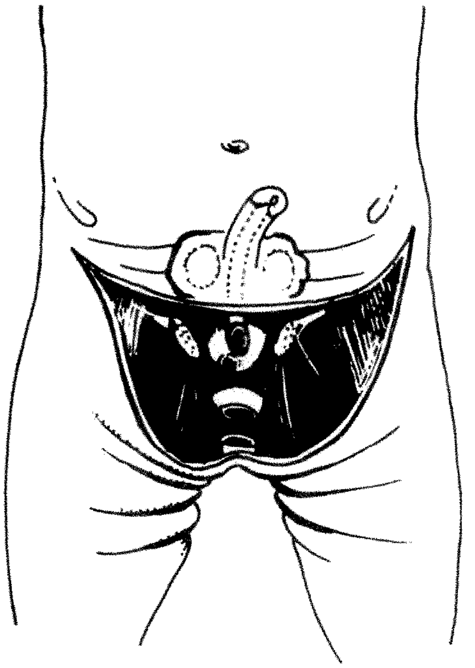


FIG. 16

The "down trousers crush injury" caused by a combination of crushing and rolling force. The pelvic ring is forced inwards, the adductor muscles are crushed and torn and the bladder, urethra and rectum are severed.

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cystostomy. No way could be found through the prostatic urethra, and a dimple was all that could be discerned of his anal canal: indeed it was difficult to introduce even a fine probe into the narrow fistula which represented what had once been the anus. We started by performing a scrotal flap urethroplasty. When this was completed, Mr A. G. Parks tackled the anus, and reconstructed that canal. We were then left with a narrow fistula which had been present before either of these operations. This was approached by dissecting in the plane between the reconstructed urethra and the reconstructed anus. There lay a narrow tube of epithelium. It was divided between ligatures and a plug of fat was interposed. Today, he is continent both of fæces and of urine.

The third and most severe of the problems which are created by injury is the result of a combined crushing and shearing injury. The result is a compression fracture of the bony ring of the pelvis with gross posterior displacement of the symphysis pubis and ischium, together with a tearing downwards not only of the skin of the perineum and thighs, but also of the adductor muscles. The whole effect is that of a macabre dropping-down of trousers (Fig. 16).

In the initial stages after the injury the patient may be nearly exsanguinated: there is an enormous raw area in the perineum and thighs; the urethra is breached, often more severely than at first appears; the rectum may be split across in part or completely and there is very extensive crushing and devitalisation of muscle. For the patient to survive demands very active treatment: massive replacement of blood must as soon as possible be supplemented by a suprapubic cystostomy and a colostomy. If the perineal wound is sutured, however loosely, the necrotic muscle and soft tissues will create a gigantic abscess in which gas gangrene all too readily takes hold and hyperbaric oxygen therapy was required in two of our cases. Ideally, delayed primary or even secondary suture would seem the best plan of treatment. Three of these injuries have been treated in our hospitals. One has been restored to complete anatomical union: *i.e.* his urethra has been repaired by means of a modified urethroplasty and his rectum and bowel made into a continuous canal again. Surprisingly, he even has control over both bowel and urine. The other 2 patients are still a long way from restoration: one is waiting for his second stage urethroplasty, the other has a neurogenic bladder in addition to a severed urethra, and it is doubtful whether any more efforts should be made to get his anatomy back to normal.

Trophic Lesions (1 case).—Last of all there is the patient who defies any kind of restorative treatment:

B. D., aged 18 (St P. 64198). This patient was born with a thoracic meningomyelocele. After prodigious efforts on the part of pædiatric surgeons he survived, and by the age of 16 was walking with the aid of a caliper. Then he developed an ulcer where the caliper chafed his groin. This would not heal. In addition, he had a congenital dislocation of the head of his right femur. It was felt that this should be excised. The wound did not heal. He developed a staphylococcal septicæmia. Finally the right lower limb was amputated through the thigh joint. The wound still did not heal. Rotation flaps were twice employed to close the gap. They did not heal. Worse, the urethra sloughed away leaving a gap 1 cm. distal to the verumontanum. Urine constantly leaked around the catheter and the whole of his perineum was converted into a vast granulating ulcer. On transfer to St Peter's Hospital it seemed that the first thing to do was establish a urinary diversion, so an ileal loop was made (Fig. 17) and subsequently the skin of the scrotum was brought down to cover the defect in the perineum. Today a small area is still unhealed.

DISCUSSION

The surgical principles which underlie the management of urethral fistulæ have been known for many centuries, and they do not change. In dealing with the commoner small fistulæ of the urethra it is only necessary to make sure that the asociated stricture is kept dilated, and the fistula will, as a rule, close spontaneously. Should it require operative closure, it may be simply excised and oversewn, provided the urine is diverted to protect the suture line for a short period of time.

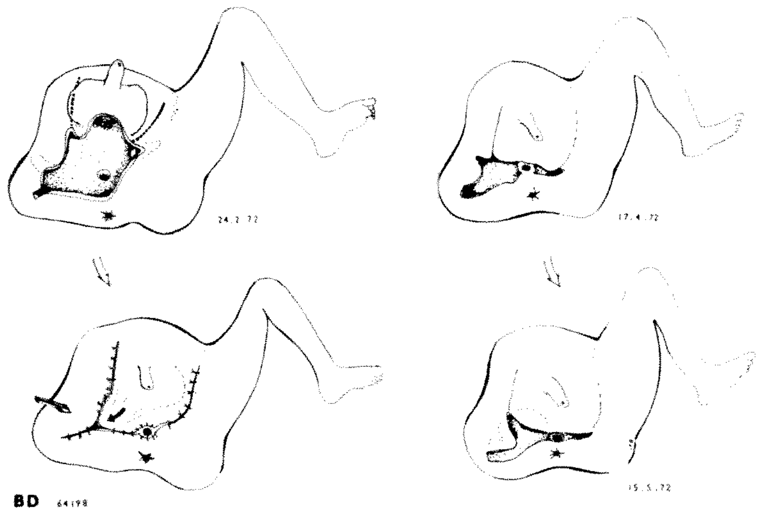

FIG. 17
A severe trophic lesion involving massive loss of the urethra by sloughing. After an ileal conduit the scrotum was swung down to try to close the gap.

In the management of the more complicated injuries which follow inflammation, certain principles would seem necessary in the management of the case.

(i) Underlying specific infection must be treated at the same time. Failure to treat co-existing tuberculosis for example may lead to failure of union of a urethroplasty.

(ii) Any large collections of periurethral pus must be drained.

(iii) The urine must be diverted suprapubically for long enough to allow the perineal tissues to lose their brawny œdema and induration.

(iv) If there is a coexisting fistula—as there nearly always will be—then it must be laid open, and an inlay urethroplasty performed.

(v) A foreign body or stone must be removed. Provided these principles are adhered to, and none of them are new, one can expect the fistula to heal. What one may also expect, it would seem from our experience, is that the patient may retain or regain continence even though there may appear to have been extensive damage to the sphincter.

In dealing with traumatic fistulæ one encounters three additional problems. The first may be the very long gap which separates the dislocated bladder from the stump of the urethra. To bridge this we suggest using a skin-lined tube derived by a modification of the scrotal-flap urethroplasty. If this is adequately treated the fistula will close on its own. Secondly, there may be an almost impenetrable stenosis of the anal canal combined with that of the urethra, with a fistula between them. Here we suggest dealing with the urethral reconstruction first, then the anal canal, and finally, if the fistula remains, closing that through a perineal approach. Thirdly we report a characteristic and massive injury of the pelvis in which not only is the skin and muscle of the thighs and perineum torn down and severely crushed, but the rectum is torn across and the urethra severed, as a consequence of a crushing and shearing injury. Such cases are likely to be met with more commonly now that modern methods of resuscitation permit more of these severely injured patients to survive the initial injury. Gas gangrene, or at least serious fæcal contamination, are a very important threat in the first days after the injury, and whenever this particular combination of injuries is suspected we suggest that suprapubic urinary diversion and a defunctioning colostomy should be established as soon as the general condition of the patient permits. The defect in the badly crushed and devitalised perineum should not be treated by primary suture.

There remain a small group of patients for which no reconstructive surgery seems appropriate, and these are patients with loss of sensation due to a neurogenic lesion. Here the best course is to provide some method of permanent diversion of urine. The scrotal skin may be found useful in assisting in the closure of the perineal defect.

Otherwise, urinary diversion remains the last resort in the management of urethral fistulæ, since, with the methods of urethral reconstruction which are available today, it should be possible in nearly every case to restore anatomical continuity to the urinary tract and get rid of urinary fistulæ, and our experience leads us to believe that continence may be regained despite the violation of what have hitherto been regarded as essential sphincter mechanisms.

It is a pleasure to acknowledge the help of many colleagues but for whose expertise many of these patients would not have survived long enough to need urethral reconstruction and in particular the authors would wish to thank Messrs D. G. A. Eadie, R. J. Luck, C. V. Mann, A. G. Parks and J. Watson.

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THE USE OF PEDICLE GRAFTS IN THE REPAIR OF URINARY TRACT FISTULAE[1]

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SIMPLE urinary tract fistulæ, particularly those involving the bladder, can usually be closed by layer suture procedures and, if the adjoining tissues are healthy, meticulous attention to surgical technique ensures a high success rate. Some fistulæ, however, present a more complex problem as a result of fibrosis, infection, irradiation, immuno-suppression, previous surgery, trauma and tissue loss; in these some form of pedicle graft is often indicated.

Scroto-Perineal Skin Pedicle Grafts.—The Denis Browne technique was developed to overcome the natural shortage of skin on the penile circumference, which is particularly critical at the base of the penis, but a tube closure creates a more even neo-urethal calibre and reduces the incidence of fistulæ. If redeployment of the foreskin during the first stage of a hypospadias repair does not provide sufficient excess of penile skin to ensure a confident tube closure without a dorsal tension-relieving incision, it is helpful at this stage to rotate a scrotal pedicle graft on to the penile shaft (Fig. 1) (Turner-Warwick, 1969*a*). This procedure also provides a reliable technique for the treatment of fistulæ following hypospadias repair.

Fistulæ related to the posterior bulbar urethra are commonly the result of traumatic injury or stricture associated with chronic infection: they usually require a two-stage repair and there are clear advantages in procedures that create a wide posteriorly placed perineal funnel through which satisfactory establishment of the inlay can be observed and, if necessary, readjusted. Perineal funnels can be achieved either by the posteriorly based perineo-scrotal flap (Leadbetter, 1960; Gil Vernet, 1967; Blandy *et al.*, 1968) or by the scrotal drop-back procedure (Turner-Warwick, 1959, 1969) (Fig. 2). The decision between these techniques is usually a simple matter of surgical preference; in some the posterior flap has clear advantages, while in others the scrotal drop-back may provide a more convenient source of skin cover if the perineal skin is compromised by fistulæ. The inflammation associated with infected and indurated "watering can" perineal fistulæ should ideally be allowed to settle as much as possible as a result of suprapubic catheter drainage for a month or two. In excising the indurated perineal tissues the scrotal skin itself should be preserved, even if it is quite extensively indurated, because, once the underlying inflammation is removed, the overlying scrotal skin tends to recover much of its natural elasticity and can often be redeployed to cover any residual skin defect some weeks later (provided of course there is no unresolved infection of specific ætiology).

When perineal skin loss is extensive, replacement has to be achieved on the basis of a "catch-as-catch-can" advancement or rotation of pedicle flaps (Fig. 3B). Those associated with extensive perineal tissue loss may require omental pedicle grafts while in others, associated with a high supra-membranous stricture, a tubed skin inlay urethroplasty may be helpful (Fig. 3A) (Anderson and Hynes, 1965; Blandy, 1971).

Local Soft Tissue Inter-position Grafts.—The majority of simple vesico-vaginal fistulæ can be closed by layer suture through a vaginal approach. While the small failure rate of these can be reduced to a minimum by meticulous technique, it can be reduced still further by the use of inter-position pedicle grafts of local tissues in appropriate cases. The addition of this procedure

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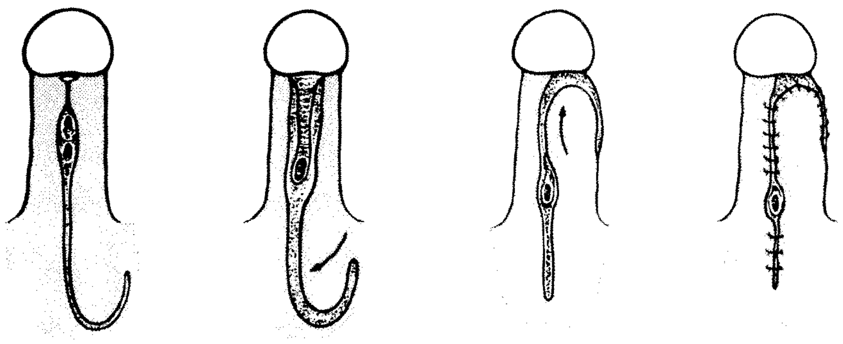
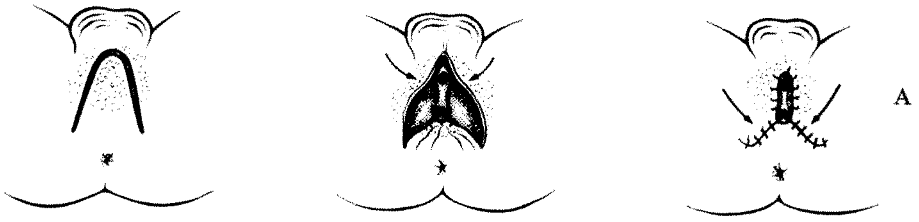
[1] Read at the Twenty-eighth Annual Meeting of the British Association of Urological Surgeons in London, July 1972.

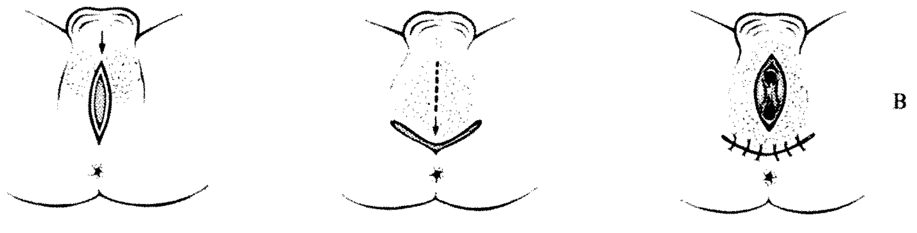


SCROTOPENILE ROTATION FLAP FOR HYPOSPADIAC FISTULA
(providing excess skin for subsequent tube closure of urethra)

FIG. 1



Posteriorly based perineo-scrotal skin flap inlay

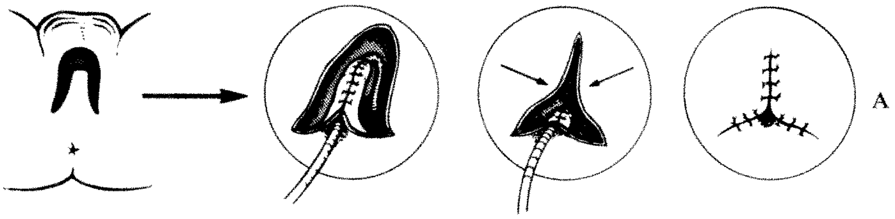


"Drop-back" scroto-urethral inlay

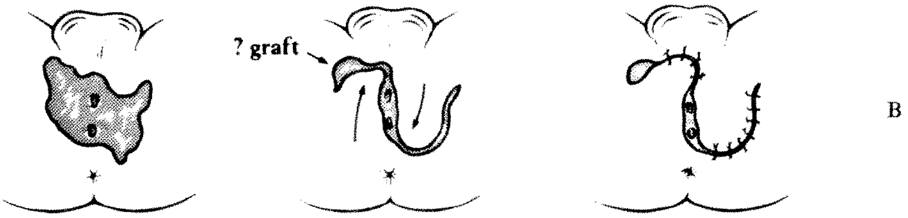
FIG. 2
Posterior funnel inlay urethroplasty.

is of course unnecessary in the majority of cases but the art of fistula repair is the anticipation of the occasional complication. If the resolution potential of a vaginal repair seems precarious, a pedicle flap of labial fat can be mobilised and interposed between the bladder and vaginal suture lines through a lateral tunnel, after the technique of Martius (Fig. 4A).

For the high vesico-vaginal fistulæ in which the abdominal approach is indicated a flat, legs-apart position provides the option of a synchronous vaginal approach. The trans-peritoneal posterior vesical approach has advantages over the trans-vesical route (Fig. 4B): It provides a good view of the relationship of the fistulæ to the ureteric orifices and to the relevant area of the posterior bladder wall in which additional fistulæ may be present. (2) The extra-vesical course of



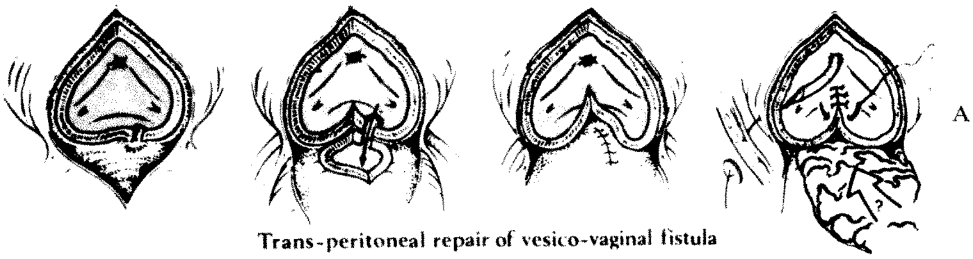
Skin-tube pedicle inlay



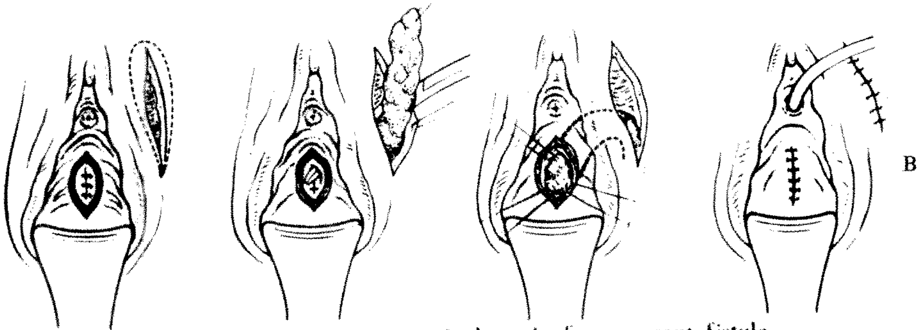
"Catch-as-catch-can" skin flaps for severe perineal laceration

FIG. 3

LOCAL TISSUE INTERPOSITION GRAFT



Trans-peritoneal repair of vesico-vaginal fistula



Labial fat pedicle supporting a vaginal repair of a recurrent fistula (Martius)

FIG. 4

Local tissue interposition pedicle grafts. A, Transperitoneal repair of vesicovaginal fistula with optional synchronous perineal approach and/or local interposition graft of omentum or peritoneum. B, Labial flap pedicle supporting a vaginal repair of a recurrent fistula.

the ureters can be identified and they can be reimplanted if necessary. (3) The inter-position of a soft-tissue pedicle flap between the closures is facilitated. A peritoneal flap often provides a useful pedicle graft but its potential is compromised if the pelvis has been irradiated; striated muscle is far from ideal since it has a very poor resistance to infection and tends to become fibrotic with disuse.

Omental Pedicle Graft.—The specific healing characteristics of the omentum associated with its specialised vascular supply and lymphatic drainage are entirely familiar but, in addition, unlike peri-renal and peri-ureteric fat, it does not develop densely fibrotic adhesions, regaining its soft and pliable character once the healing process is complete.

It is thus particularly useful for supporting the more difficult repairs and reconstructions of both upper and lower urinary tracts; not only does it speed the resolution of infective processes and the repair of tissue defects, but it also enables a reconstructed ureter or bladder to regain its intrinsic mobility without becoming frozen to the surrounding tissues; furthermore it provides a useful tissue plane should a re-exploration become necessary.

Omental Graft to the Upper Urinary Tract.—A limited mobilisation is sufficient to enable the omentum to reach the kidney and abdominal ureter and this can usually be accomplished quite easily, in the course of a loin approach to the upper urinary tract, through a small peritoneal incision immediately lateral to the colon. After freeing any incidental adhesions all that is usually required is separation from the transverse colon in the avascular plane and the division of the apron vertically, between suitable vertical branches of the gastro-epiploic vessels; it is rarely necessary to divide the short gastric branches.

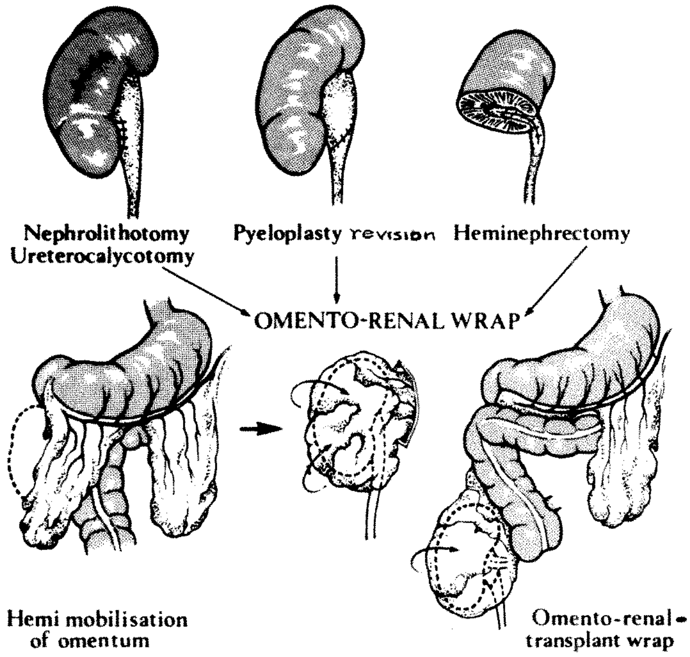


FIG. 5
The omento-renal wrap.

We use an omental wrap as a routine to support some of the more difficult renal operations such as nephro-lithotomy, staghorn calculi, uretero-calycostomy, re-exploration for post-pyeloplasty obstruction, heminephrectomy etc. (Fig. 5). It is difficult to achieve objective evaluation of the results of this but so far as we know we have had no complications from its use and feel justified in attributing to it our very fair measure of freedom from post-operative complications following some of the more heroic reconstructive procedures.

We have occasionally re-explored omental-wrapped upper urinary tracts for recurrent stone or for revision of reconstructive procedures; on each occasion the relative ease with which the tissue planes could be re-identified was quite remarkable (Worth and Turner-Warwick, 1971). The omental wrap has been used to close fistulæ resulting from renal transplantation and we have previously suggested that it might be useful in the prevention, not only of fistulæ but also of the frozen adhesions around its vascular pedicle, which compromise any re-exploration (Turner-Warwick *et al.*, 1967).

OMENTO-URETERIC WRAP

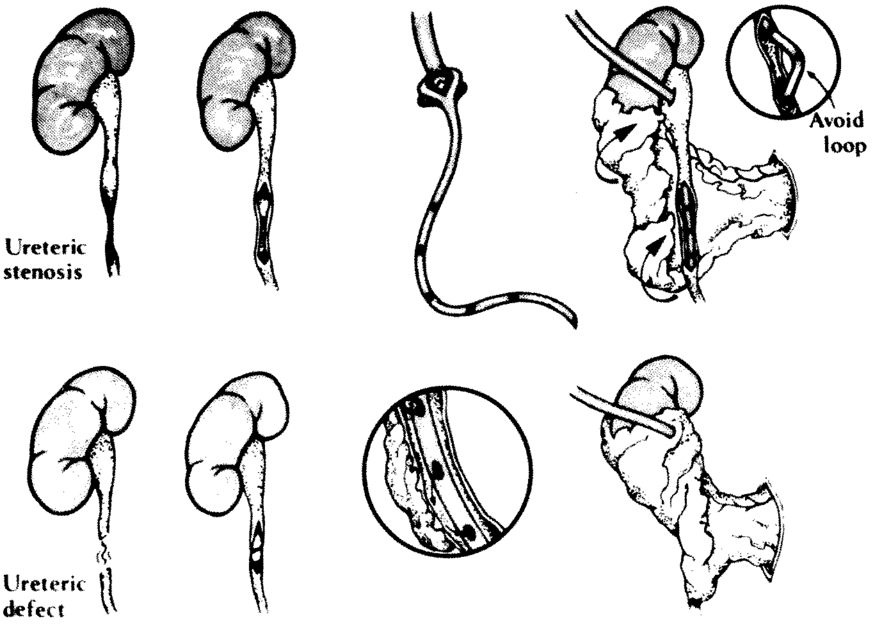


FIG. 6

The omento-ureteric wrap. Support for ureteroplasty and ureterotomy procedures and the use of the Cummings catheter with a fenestrated splinting tail.

The omento-ureteric wrap is particularly useful for the support of an extensive ureteroplasty (Fig. 6) and we have also used it in the support of reconstructive procedures that had to be undertaken for tuberculosis before the disease had been properly controlled (Turner-Warwick, 1970).

We have been particularly impressed by the value of an omental wrap as a routine support for intubated Davies ureterotomy; the healing time seems to have been shortened so that we usually remove the splinting catheter, after the check ureterostography, about the end of the third week. We have a personal preference for a Cummings catheter inserted as a pyelostomy with the tail transversing the ureteroplasty; whatever form of ureterostomy tube is used, however, we feel that multiple fenestrations contribute significantly to the success of the procedure in that they provide free drainage for the exudates which may otherwise accumulate in the peri-catheter space and compromise healing (Turner-Warwick 1972). It is, of course, particularly important that the splinting catheter should lie approximated to the ureter and not form a loop which would allow the ureter to roll up and create a narrow tube in the interval (Fig. 6).

Omental Pedicle Graft to the Lower Urinary Tract.—Only the lower fringe of the omentum will normally reach the pelvic cavity and definitive mobilisation is usually necessary for it to do so. The use of the omentum for vesical fistulæ was pioneered by Bastiaanse (1954 and 1960) who used a limited mobilisation procedure; definitive mobilisation, based on the right gastro-epiploic vessels, depends upon the careful individual ligation of all its short gastric branches with absorbable ligatures (Fig 7A); the technique of this has been previously described elsewhere, together with its various applications (Turner-Warwick *et al*, 1967); It is particularly important to be aware that even if the vertical extent of the omental apron is relatively short, as it commonly is in children, definitive mobilisation of the full length of the gastro-epiploic vessels along the greater curvature of the stomach usually provides sufficient mobilisation for an effective omental support, even for a urethral reconstruction (Fig 7A).

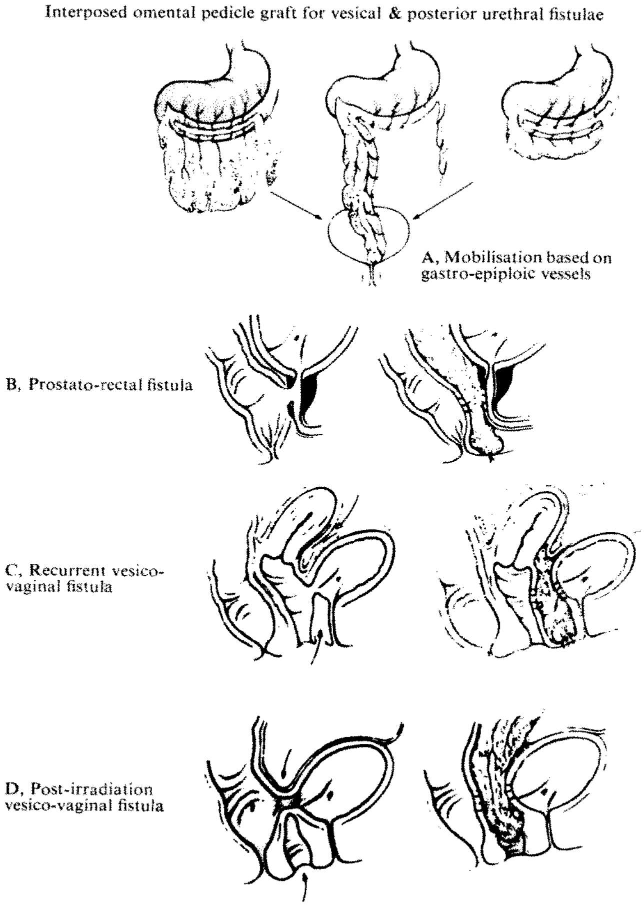

Interposed omental pedicle graft for vesical & posterior urethral fistulae
A, Mobilisation based on gastro-epiploic vessels
B, Prostato-rectal fistula
C, Recurrent vesico-vaginal fistula
D, Post-irradiation vesico-vaginal fistula

FIG. 7

The inter-position pedicle graft for vesical and posterior urethral fistulæ. A, Mobilisation based on right epiploic vessels; the length potential of the "short" omentum. B, Prostato-rectal fistula. C, Recurrent vesico-vaginal fistula. D, Post-irradiation of vesico-vaginal or vesico-vagino-rectal fistulæ.

Omental inter-position provides a remarkably reliable technique for the closure of prostato-rectal fistulæ even when previous attempts have failed. Having established a proximal sigmoid colostomy, an abdomino-perineal tunnel is created between the rectum and the urinary tract;
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it is important that this should be adequately developed laterally to accommodate three to four fingers in order to ensure a substantial inter-position; the rectal defect is closed with a single suture layer but it is often impossible to close the prostatic urethra accurately, and this can be safely left open with a fenestrated splinting catheter in apposition to the omental graft.

The technique of simple inter-position is also valuable for recurrent or moderately complicated vesico-vaginal fistulæ; again it is particularly important to achieve a three to four fingers' breadth abdomino-perineal tunnel, not only to provide space for an adequate bulk of interposition but also to ensure that there are no subsidiary lateral fistulous tracks. If such a repair is undertaken for a potentially childbearing patient, care should be taken to bring the pedicle of the omental graft to the fistulous site in an extra-peritoneal tunnel in order to prevent the ovaries and tubes from becoming enveloped within it (Fig. 7C).

The technique of omental closure is particularly suited to the repair of extensive post-irradiation fistulæ and the success rate with this vascular graft is remarkably high, even in the presence of severe irradiation changes. The procedure has to be adapted to each particular case. When the residual vaginal vault is frozen and stenotic, as it was in the vesico-vagino-rectal fistula illustrated in Figure 7D, it is important to remove its epithelial lining in order to prevent it forming a persistent fistulous tract; the omental inter-position can be included in the suture line of the relatively unaffected vaginal cuff.

Fistulae Associated with Gross Tissue Loss.—Bulbar urethral fistulæ resulting from trauma are often associated with extensive loss of perineal tissues. Several important principles are illustrated in Figure 8. A suprapubic catheter was inserted: the patient remained incontinent and sphincter incompetence was feared, the urinary leakage, however, proved to be due to an anterior retropubic fistula, by-passing the sphincter mechanism. At the time the patient was referred his perineal fistula had been epithelialised for more than a year and it was therefore possible to mobilise the proximal and distal ends of the anterior urethra, leaving a tongue of skin on each to achieve an overlapping anastomosis with a fenestrated catheter drainage. The urethral anastomosis was supported by a double omental pedicle graft brought down both in front and behind the bladder, and a perineal skin closure was achieved by a scrotal drop-back. Another patient illustrating the reconstructive value of the omental pedicle graft is shown in Figure 9; a cloacal post-traumatic perineal injury involving loss of the anterior rectal wall and the posterior part of the lower prostate, the membranous and the posterior bulbar urethra. Reconstruction was performed using an anterior rectal pull-through, an abdomino-perineal inter-position omental graft and a scrotal drop-back urethroplasty, thus creating an effectively bulky recto-urethral septum: the intact pubo-rectal sling provided rectal continence and the intact bladder neck maintained urinary continence.

Extensive repair of the posterior urethra inevitably compromises the sphincter mechanism in some degree. Continence can be expected if either the bladder neck or the distal urethral mechanism is intact; if both these are impaired, continence may be compromised. The extent of sphincter dysfunction is often difficult to assess pre-operatively and when this is questionable it is usually advisable to proceed with the initial repair and re-evaluate the problem thereafter: one-stage procedures facilitate urine collection should this be necessary.

Vesical Tube Replacement of the Lower Ureter.—The pelvic ureter can be replaced by vesical tube pedicles. The Boari bladder flap procedure is widely used but the relatively simple psoas bladder-hitch procedure has certain advantages (Fig. 10). (Turner-Warwick and Worth 1969), and it is particularly easy to achieve a reflux preventing reimplantation of one or both ureters. The procedure was, in fact, first advocated for the repair of a uretero-vaginal fistula (Zimmerman *et al.*, 1960).

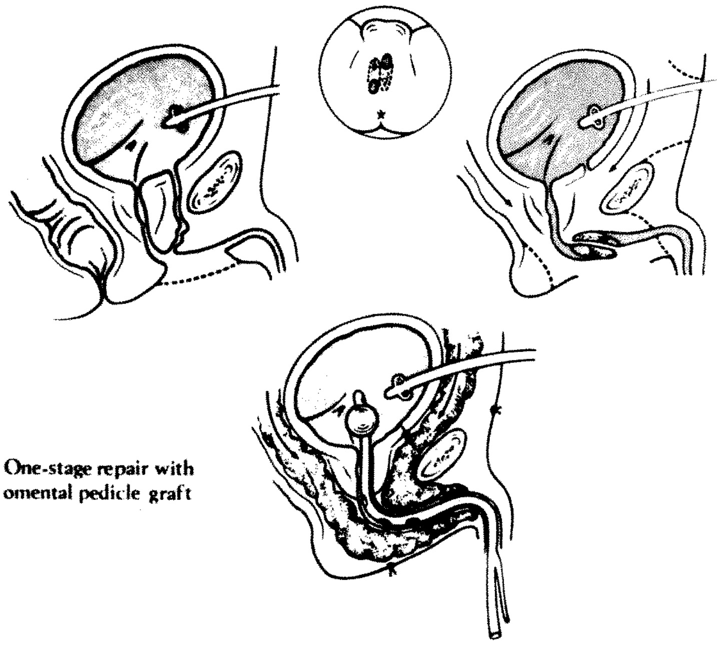


FIG. 8

One-stage repair of post-traumatic anterior urethral fistulæ with omental pedicle wrap.

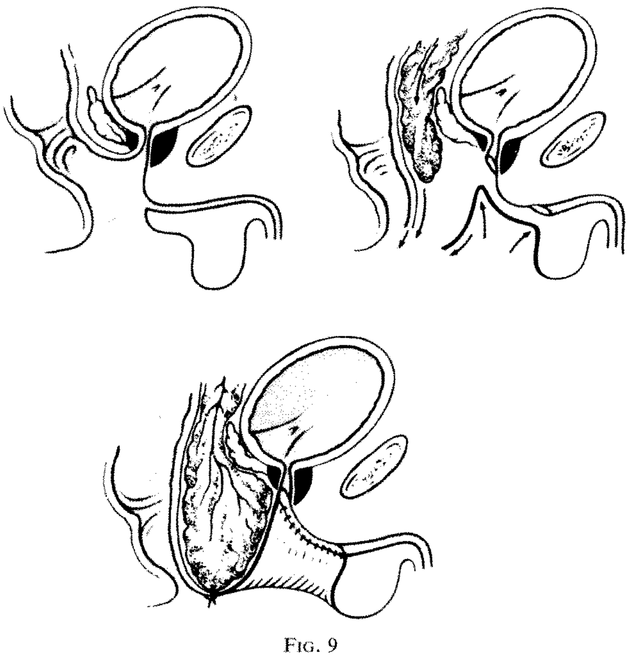


FIG. 9

Omental reconstruction in traumatic tissue-loss cloacal injuries. Anterior rectal wall "pull-through", septal reconstruction with omentum and scrotal drop-back inlay urethroplasty, bladder neck and rectal continence.

PSOAS HITCH

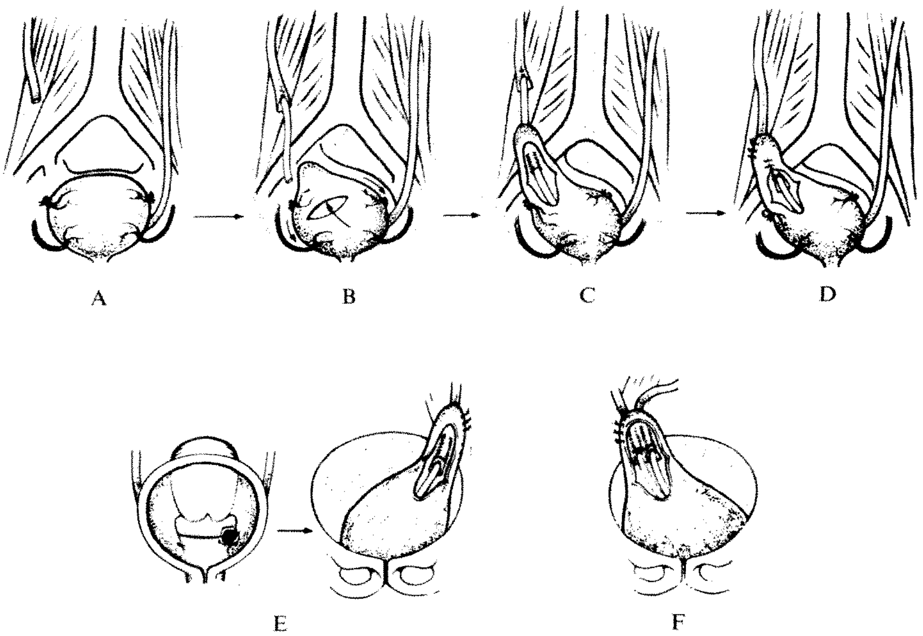


FIG. 10

The psoas-hitch replacement of the lower ureteric fistulae and strictures. A Division of superior vesical vessels. B, Horizontal bladder incision and mobilisation to base. C, Elevation of bladder. D, Psoas hitch and ureteric reimplantation. (Horizontal bladder incision closed vertically increases extent of bladder elevation.) E, Repair of uretero-vaginal fistula. F, Reimplantation of both ureters into psoas hitch.

Island Skin and Urothelial Pedicle Graft Repairs of Urinary Fistulæ.—Island skin and urothelial grafts provide the opportunity for repair of urinary fistulæ in selected cases and tend to be under-used.

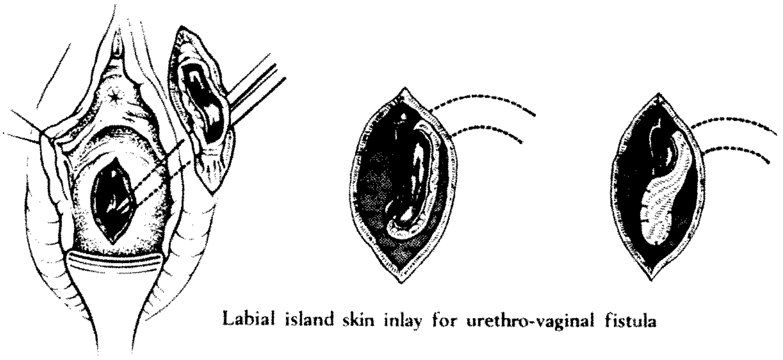
Urethro-vaginal fistulæ associated with urethral defects can be conveniently repaired by leaving an island of labial skin on a labial-fat pedicle graft (Fig. 11A). (Turner-Warwick, 1971). The procedure is similar to the Martius repair except that an island of labial skin is prejudged in position and is sutured to the margins of the urethral defect, forming its posterior wall.

A similar island-pedicle graft, formed from the anterior penile or foreskin, can be used as a basis of a one-stage repair in selected cases of anterior urethral stricture (Fig. 11B) (Leadbetter and Leadbetter, 1962; Orandi, 1972).

A ureteric defect at the pelvic brim presents a particular problem if it is too long to enable an end-to-end anastomosis to be achieved; while some of these can be resolved by a psoas-hitch procedure or an uretero-ureterostomy, it is occasionally helpful to use a bladder flap bearing an island of urothelium to bridge the defect, and to support this with an omental wrap (Fig. 12). The particular advantage of this, over a psoas hitch or Boari procedure is, of course, that the normal, reflux-proof uretero-vesical junction is preserved.

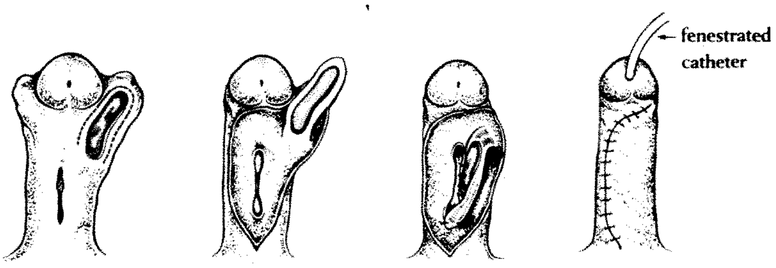
A similar "urothelial-island" bladder flap can be used to reconstruct the membranous urethra (Fig. 13); the particular advantage of this type of procedure is that a normally functioning bladder-neck mechanism is not compromised as it is with tube reconstruction, (Flocks and Culp, 1953) Figure 13E. It is perhaps not universally appreciated that the normal bladder-neck mechanism is not only capable of maintaining continence after a trans-sphincter repair of the distal

ISLAND SKIN GRAFT



Labial island skin inlay for urethro-vaginal fistula

A



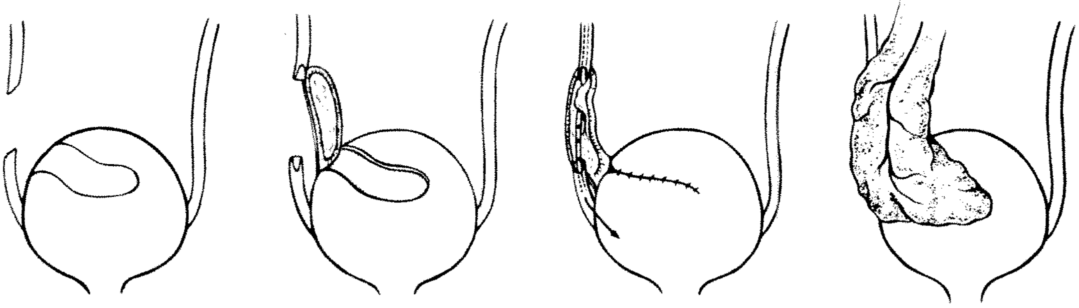
Island skin inlay for one stage repair of urethral stricture or fistula

B

FIG. 11

"Island skin" grafts. A, Labial "island skin" inlay for reconstruction of urethra associated with urethro-vaginal fistula. B, "Island skin" inlay for one-stage repair of penile strictures or fistula (foreskin or penile skin preferable to scrotum).

'UROTHELIAL ISLAND' Bladder flap ureteroplasty preserving uretero-vesical mechanism



Ureteric defect high in pelvis

A

Bladder flap with urothelial island

B

Urothelial bridge & fenestrated catheter

C

Omental wrap

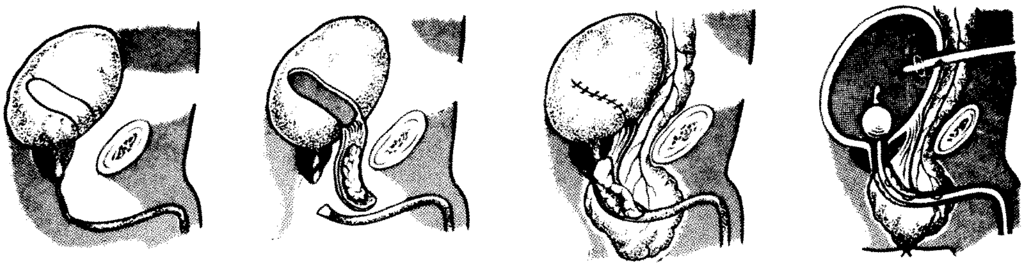
D

FIG. 12

"Urothelial island" bladder flap urethroplasty preserving the lower ureter and uretero-vesical junction. A, Ureteric defect at pelvic brim. B, Bladder flap with "urothelial island". C, Island bladder flap rolled around fenestrated splint to replace ureteric defect. D, Omental ureteric wrap.

urethral mechanism but the patients may even learn to interrupt their voiding stream by inhibiting their detrusor/trigonal mechanism and consequently closing their bladder neck. A normally functioning bladder-neck mechanism should, therefore, never be violated and a tubed vesical-pedicle graft urethroplasty is therefore only advisable if the bladder-neck mechanism is already compromised. Occasionally a tubed-bladder flap may succeed in recreating a competent sphincter-substituting mechanism (Thompson, 1963 and Tanagho *et al.*, 1969), but the occlusive function of these is not entirely reliable.

'UROTHELIAL ISLAND' Bladder flap urethroplasty preserving bladder neck mechanism



A, Long supramembranous traumatic stricture

B, Abdomino-perineal island urothelial bridge

C, Omental wrap

D, Intact bladder neck

'BLADDER TUBE' urethroplasty

E, Bladder neck destroyed

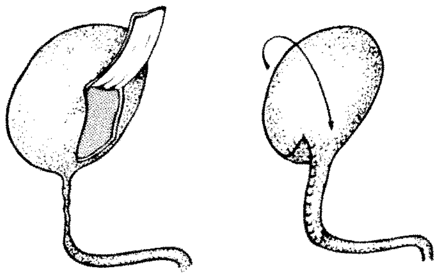


Fig. 13

"Urothelial island" bladder flap urethroplasty with preservation of bladder neck mechanism. A, Long supramembranous stricture or fistula. B, Urothelial-island bladder flap raised to bridge the urethral defect. C, Omento-urethral wrap. D, Fenestrated urethral catheter and suprapubic drainage. E, Simple bladder tube posterior urethroplasty compromises the bladder-neck mechanism.

In the event that a lower tract fistula cannot be repaired it may be possible to fashion a conduit from an island-graft formed from the bladder dome, based on the superior vesical vessels, thus avoiding the need to use an ileal segment (Turner-Warwick, 1969B).

Bowel Pedicle Grafts.—*Appendix Ureteroplasty.*—The use of the appendix for the replacement of a segment of the ureter (Fig. 14A) has been described by Wesolowski (1971). We have no experience of this as a circumferential graft but have once used the opened appendix as a pedicle patch graft.

Bowel Ureteroplasty.—The replacement of a damaged ureter by a segment of bowel has been advocated by many authors but it may result in a urodynamically compromising situation involving free reflux into a capacious neo-ureter which in turn compromises the voiding efficiency of the bladder (Fig. 14B); this vesico-neo-ureteric reflux can be prevented by a "no-tunnel" cuff-nipple anastomosis (Fig. 14D). Replacement of both ureter and bladder by a bowel segment is a relatively reliable procedure provided the voiding mechanism is re-balanced (Turner-Warwick and Handley Ashken, 1967) (Fig. 14c). In order to prevent reflux the free-hanging intravesical nipple of a "no-tunnel" reimplantation needs to be twice as long as it is wide (Turner-Warwick and Worth, 1969). The split-cuff nipple of a mega-ureter or bowel reimplantation is consequently quite large but nevertheless effective; the bladder should, however, be anchored laterally, at the point of entry, in order to prevent ball-valve obstruction by the nipple at the bladder neck as the bladder empties.

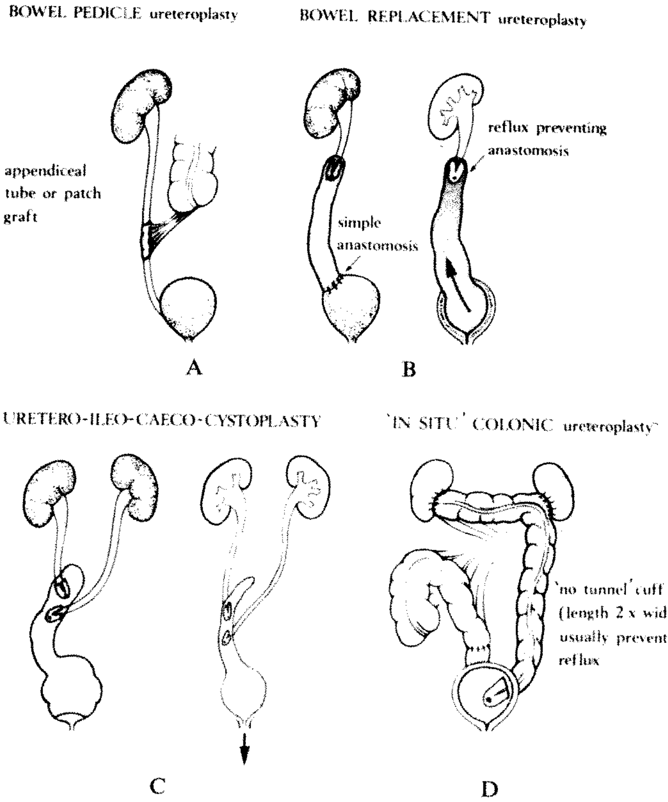

BOWEL PEDICLE ureteroplasty
BOWEL REPLACEMENT ureteroplasty
appendiceal tube or patch graft
reflux preventing anastomosis
simple anastomosis
A
B
URETERO-ILEO-CAECO-CYSTOPLASTY
'IN SITU' COLONIC ureteroplasty
'no tunnel' cuff nipple (length 2 x width) usually prevents reflux
C
D

FIG. 14

Bowel pedicle ureteroplasty. A, Appendiceal ureteroplasty—tube or patch graft. B, Ileo-ureteroplasty may be compromised by vesico-"neo-ureteric" reflux. C, Bowel replacement of ureter and bladder is functionally efficient if the outflow is balanced or rebalanced. D, Bowel replacement of ureter with reflux-preventing "no tunnel" cuff nipple anastomosis (*in situ* colonic replacement sometimes preferable to ileum).

CONCLUSION

While the majority of relatively simple fistulæ can be closed by a simple layer-closure technique, the use of inter-position and replacement grafts greatly improves the success rate in the potentially complicated cases. This contribution reviews some of the pedicle grafts that have been used to resolve the more difficult fistulæ.

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British Journal of Urology (1972), 44, 657-661

GENITO-URINARY FISTULÆ COMPLICATING CROHN'S DISEASE[1]

By Patrick J. B. Smith, R. E. Williams
and A. T. DeDombal

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Four years after the original description of Crohn's disease (Crohn *et al.*, 1932) the first associated bladder fistula was recorded (Ten Kate, 1936).

Sporadic accounts of individual cases of genito-urinary fistula in Crohn's disease followed and in 1969 Kyle and Murray in an extensive review of the subject were able to quote 97 cases from the world literature, to which they added 10 cases of their own. More recently Hira (1970) has reported on the management of 5 cases of urinary fistula complicating Crohn's disease.

That genito-urinary fistula is not a common complication of Crohn's disease is born out by a study of the literature. The largest series, from the Mayo Clinic, showed an incidence of such fistulæ in 600 cases of Crohn's disease to be 1·6 per cent (Van Patter *et al.*, 1954). At the Cleveland Clinic the incidence was 1 per cent (Daffner and Brown, 1958), in Mount Sinai Hospital 2·2 per cent (Crohn, Yarnis, 1958). The series mentioned above by Kyle and Murray in 1969 showed an incidence of 2·2 per cent and an earlier paper from Leeds (Atwell *et al.*, 1965) gave 4·9 per cent as the incidence of genito-urinary fistula in Crohn's disease. The highest figure, 8·5 per cent, was reported from Norway (Gjone *et al.*, 1966).

This paper is divided into two sections. The first, the Leeds Survey, is a study of the incidence of genito-urinary fistulæ in 332 patients with Crohn's disease presenting in the Department of Surgery of the University of Leeds over the past 34 years.

The incidence of all complications in these 332 patients is listed in Table I and shows that fistula occurrence is the second commonest complication of Crohn's disease. The 24·4 per cent rate listed represents all types of fistula, both internal and external, but if the cases of genito-urinary fistula are treated separately, they are found to occupy 4·2 per cent of the total complication rate representing 14 fistulæ in the 332 patients (Table II).

These fistulæ occupy varying anatomical sites as shown in Table III. Ileo-vaginal fistulæ are very rare and only 12 cases have been recorded in the world literature (Kyle and Sinclair, 1970). These figures confirm that in this series the incidence of genito-urinary fistulæ, as in the other series listed above, occupy a small place in the complication rate of Crohn's disease.

However, the Leeds series includes many cases referred from outside the unit which, because of its special interest in the subject of Crohn's disease, often attracted more complex cases and hence may represent a selected series. In order, therefore, to get a clearer idea of the management of these fistulæ it was decided to extend this paper into a second section, in which is included another 8 cases of genito-urinary fistula in Crohn's disease presenting in the Sheffield hospitals. These cases are mentioned elsewhere (Moisey and Williams, 1972) and our thanks are due to them for permission to quote certain clinical details in this paper. With the addition of these 8 cases a total of 22 cases is analysed. There were 13 males and 9 females (Table IV), a ratio in accordance with that described by Kyle and Murray (1969). The age at the onset of the fistula covered a wide range (Table V), with an average age of 41·5 years, a figure somewhat higher than the 34 years of Kyle and Murray (1969).

Symptoms of Crohn's disease had been present from 3 months to 20 years prior to the onset of the fistula (Table VI) and in 4 cases the occurrence of the fistula was the presenting feature of Crohn's disease. These figures suggest that the occurrence of a genito-urinary fistula in Crohn's disease does not necessarily imply a long-standing or severe type of Crohn's disease. However, in those cases with established Crohn's disease 7 had required an operation for "ileitis" before developing their fistula. In none of these was the fistula formation apparently related to the surgery but it is interesting to note that all 7 cases were from the Leeds series, representing 50 per cent of that total, whereas none were from the 8 Sheffield patients, emphasising the more selective nature of the Leeds cases.

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[1] Read at the Twenty-eighth Annual Meeting of the British Association of Urological Surgeons in London, July 1972.

TABLE I

Complications of 332 Cases of Crohn's Disease (Leeds 1938/70)

	Percentage
Perianal	42·5
Fistula	24·4
Stricture	10·5
Obstruction	21·7
Eye	6.9
Skin	6·9
Joint	9·0
Mouth	6·6
Anæmia	14·5
Malabsorption	18·7

TABLE II

Genito-urinary Fistulæ in Crohn's Disease (Leeds 1938/70)

Total cases of Crohn's disease	332
Genito-urinary fistulæ	14
Percentage incidence	4·2

TABLE III

Anatomical Site of Fistulæ (Leeds 1938/70)

Ileo-vesical	8
Ileo-colo-vesical	4
Recto-urethral	1
Ileo-vaginal	1
Total	14

TABLE IV

Genito-urinary Fistulæ in Crohn's Disease (Leeds/Sheffield)

Leeds cases	14
Sheffield cases	8
Total	22 (13 male, 9 female)

Information relating to the presenting symptoms of the fistula is listed in Table VII. All the patients had abdominal symptoms of pain, diarrhœa and weight loss to a varying degree. In 1 patient with an ileo-vaginal fistula there were no urinary symptoms. As can be seen, frequency and dysuria were the commonest complaints, with fæcaluria and pneumaturia next in order of importance. One patient developed acute retention and 1, with a recto-urethral fistula, complained of passing urine per rectum ("urorrhœa"). None of these patients complained of hæmaturia. Physical signs were not much in evidence, most of the patients had lower abdominal tenderness, especially on the right side, and in 2 there was a palpable mass. In 4 patients there was other evidence of underlying disease with three healed fistulæ-in-ano and one active suprapubic cutaneous fistula.

Table V

Age at Onset of Fistula (Leeds/Sheffield)

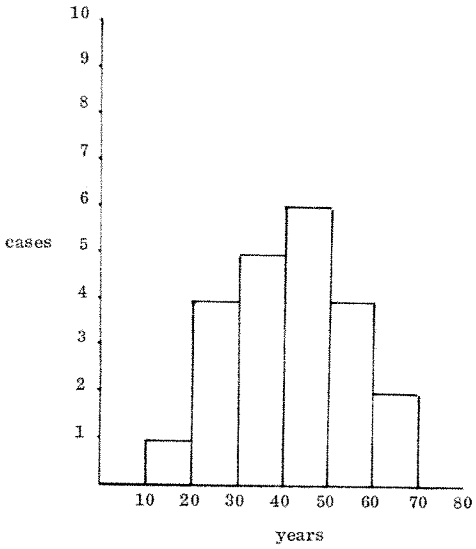

Table VI

Duration of Crohn's Disease prior to Onset of Fistula (Leeds/Sheffield)

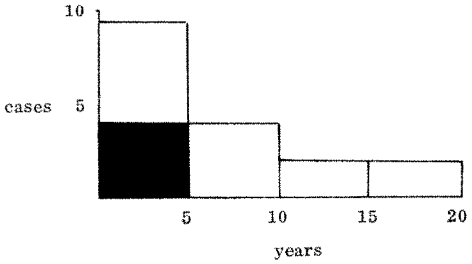

Table VII

Presenting Symptoms of Fistulæ in 21 Patients (Leeds/Sheffield)

	Patients
Frequency and Dysuria	16
Pneumaturia	11
"Fæcaluria"	9
"Urorrhoea"	1
Retention	1

Table VIII

Investigations for Fistulæ in 21 Patients (Leeds/Sheffield)

	Total performed	*Positive result*
Urine culture	16	16
I.V.P.	10	0
Cystogram	2	2
Cystoscopy	10	6
Barium meal and follow-through	6	2
Barium enema	11	3

Investigations of these 22 cases were many and varied, representing the polyglot nature of the clinicians involved; those investigated by urologists or surgeons or gastro-enterologists all showing the different diagnostic emphases of these specialities (Table VIII). The commonest finding was of infected urine with *B. coli* as the usual organism. Barium studies were not very helpful in diagnosing the fistula though they did aid in the diagnosis of the underlying Crohn's disease. Two of the barium meal and follow-through examinations showed the typical sinous tracts leading from the diseased ileum to the bladder, and similarly three of the barium enemas showed the connection between bowel and urinary tract when the large bowel was involved. I.V.P. examination showed a mild degree of obstruction to the right ureter in the bony pelvis in 3 of the 9 examinations. This finding is recognised in Crohn's disease (Goldman and Glickman, 1962) but it is not diagnostic of a urinary fistula. The value of cystograms has been questioned by Kyle and Murray (1969), but it is interesting to note that two were successful on the occasions when they were attempted in this series. Cystoscopy revealed evidence of a fistula in 6 out of 10 examinations. The changes in the bladder are typically localised to the vault and vary from slight reddening of the mucosa to an œdematous polypoidal area or, rarely, the presence of an observable fistula with gas or fæcal material extruding. Kyle and Murray (1969) described the results of endoscopy as unrewarding, but this study tends to support the work of Couris and Block (1963), who described cystoscopy as the most reliable diagnostic procedure for establishing the presence of intestino-vesical fistulæ.

TABLE IX

Treatment (Leeds/Sheffield)

	Success	*Recurrence*
First Operation		
Resection	11	3
By-pass	2	0
Direct Closure	4[1]	0
Ileostomy	1[2]	0
Second Operation		
Resection	3	0

[1] Two patients required subsequent surgery for ileitis.
[2] Fistula re-opened after ileostomy closed.

Finally, it does appear from a study of these cases that, apart from the local lesion in the region of the fistula, there is no associated morbidity in the urinary tract, in particular the kidneys. Indeed, at the time of operation it is often difficult to demonstrate the fistulous opening in the urinary tract, due to the disproportionate extent of the intestinal disease.

Treatment was surgical in all but 1 case who died before surgery could be commenced. In the remaining 21 cases the operative procedures carried out are listed in Table IX.

The commonest operative procedure was resection of the diseased segment of bowel and, where feasible, direct closure of the urinary tract epithelim. This was successful in 11 out of 14 cases where it was used as the first operation. A primary closure of the fistula, without resection, was attempted on 4 patients and was successful in curing the fistula, but in 2 of these patients the subsequent progression of the Crohn's disease required further bowel surgery. One patient with a recto-urethral fistula was "cured" by an ileostomy. He subsequently had the ileostomy closed, whereupon the fistula reopened. He declined further surgery.

There were 3 patients whose fistulæ recurred; all had previously had a resection and after a further more extensive resection all 3 were cured of their fistulæ.

CONCLUSIONS

These findings suggest that a genito-urinary fistula may occur in patients with Crohn's disease at any age and at any stage of the disease process. Lower urinary tract symptoms with associated urinary infection in patients with proven or suspected Crohn's disease should raise the possibility of the diagnosis of a fistula, and pneumaturia or fæcaluria will confirm it. Cystoscopy appears to be the most useful means of diagnosis, and resection of the diseased bowel the treatment of choice. Genito-urinary fistulæ in Crohn's disease have very little associated morbidity in the genito-urinary tract. They remain a rare complication of an uncommon disease seldom encountered by the urologist.

We would like to reiterate our thanks to Mr J. Williams and Mr C. Moisey for help on the presentation of the Sheffield cases and also to Professor Goligher for his help and encouragement in the presentation of the Leeds series.

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VESICO-INTESTINAL FISTULÆ[1]

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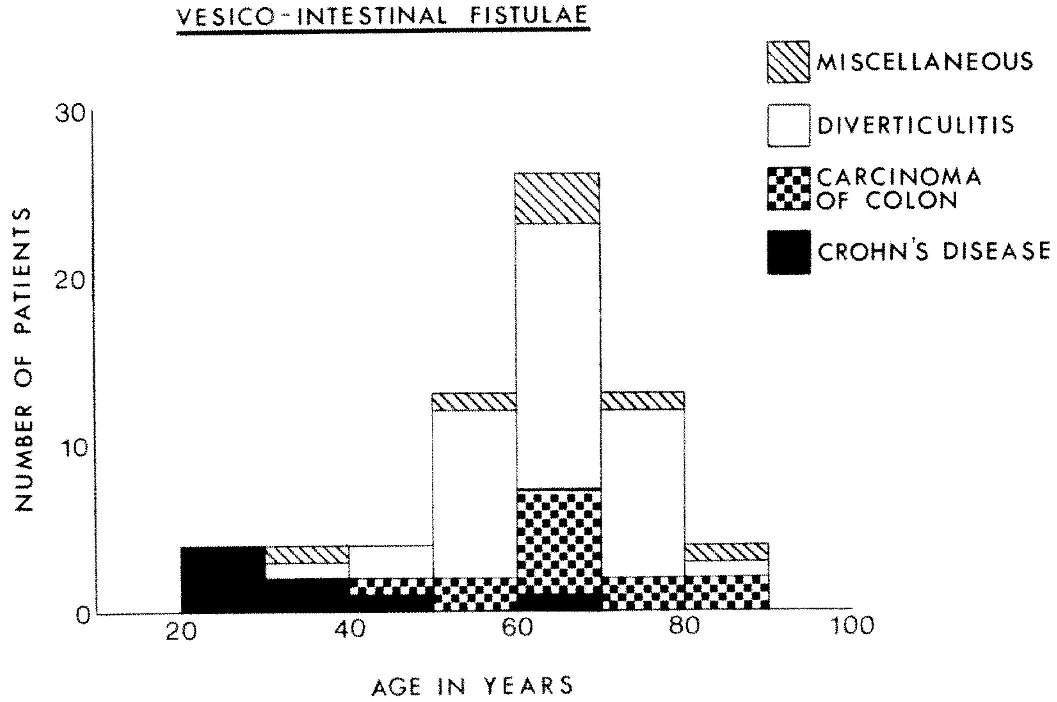
FISTULÆ between the intestinal tract and the urinary bladder are uncommon and are usually secondary to intestinal disease. The first recorded case was in the second century A.D. by Rufus of Ephesus (Pascal, 1899; Kellog, 1938), and the first serious analysis of the problem by Cripps (1888).

TABLE I



Sixty-eight patients treated between 1945 and 1972 have been collected from the Sheffield region. There were 48 males and 20 females, the ages ranging from 21 to 84 years. The causes of the fistulæ were Crohn's disease of the small bowel (8), diverticulitis (40) and carcinoma (13) of the colon and a miscellaneous group (7) (Table I).

The 7 fistulæ in the miscellaneous group (Table II) occurred as a pre-terminal event except in the case of the patient with the iatrogenic fistula which healed spontaneously after a defunctioning colostomy. These patients have been excluded leaving 61 to assess.

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[1] Read at the Twenty-eighth Annual Meeting of the British Association of Urological Surgeons in London, July 1972.

TABLE II

Miscellaneous Causes

Age	Sex	Diagnosis
84	F	Ca. cervix. Radiotherapy
40	F	Ca. cervix. Radiotherapy
38	F	Ca. cervix. Radiotherapy
67	M	Ca. bladder
63	M	Ca. bladder
74	M	Ca. prostate
65	M	Iatrogenic

TABLE III

Presenting Symptoms

	Crohn's Disease (8)	Diverticulitis (40)	Carcinoma Colon (13)
Urinary infection	2	25	10
Pneumaturia	3	29	7
Fæcaluria	5	16	4
Bowel symptoms	6	7	7

Symptoms.—The majority of the 61 patients presented with frequency, painful micturition and pneumaturia, hæmaturia being uncommon. Associated bowel symptoms were common in Crohn's disease and carcinoma of the colon, but not in diverticulitis. (Table III).

Investigations.—The urine was infected in 38, sterile in 10 and not recorded in 13 patients. Of the 10 patients with sterile urines, 9 had had antibiotics and 1 had a defunctioning colostomy.

The intravenous pyelogram was normal in all but 1 patient who showed a fluid level in the bladder.

Alimentary tract radiology was performed in 52 patients. The underlying lesion was demonstrated in 51. The other patient had Crohn's disease of the ileum and only a barium enema, with normal findings, was done before laparotomy. The fistula was demonstrated in 15 patients and in 4 a fluid level in the bladder was seen during the examination (Fig. 1). Sigmoidoscopy occasionally allowed biopsy of the colonic carcinoma, but was not otherwise helpful.

Cystoscopy was performed in 31 patients. The fistula was confirmed in 8 and a suspicious lesion seen in 22. The changes were œdema, inflammatory exudate and ulceration usually localised to the left side of the bladder vault.

Treatment.—The treatment and results in our patients with Crohn's disease are included in the Leeds series (Smith and Williams, 1972) (see p. 657). Fifty-three patients with vesicocolic fistulæ remain for appraisal and are divided into four groups.

1. 'Medical' Group.—Six patients had no operation. Four patients with diverticulitis had few symptoms and were treated symptomatically over several years with no obvious deterioration. Two patients with carcinoma of the colon died soon after admission.

2. Colostomy Group.—A defunctioning colostomy only was performed in 13 patients. Five

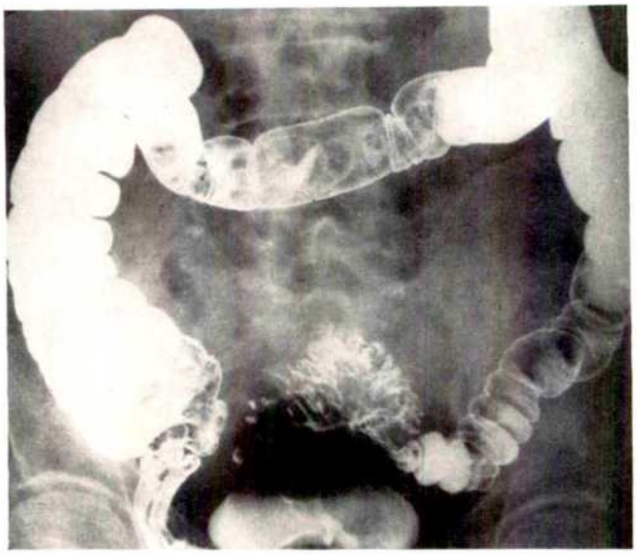

FIG. 1

patients had inoperable carcinoma of the colon. Of the 8 patients with diverticulitis, 5 were in very poor general medical condition and would not have survived further intervention, 2 died in the early post-operative period due to medical causes and 1 patient is awaiting admission for further surgery.

3. Multi-Stage Group.—In 15 patients with diverticulitis and 3 with carcinoma of the colon, a preliminary defunctioning colostomy was performed. After a period of 3-6 months the lesion and fistula were excised with subsequent closure of the colostomy.

4. One-Stage Group.—In 13 patients with diverticulitis and 3 with carcinoma of the colon, a primary excision of the lesion and fistula with end-to-end bowel anastomosis was performed.

RESULTS

Multi-Stage Group.—There was one post-operative death in a patient with chronic myeloid leukæmia. Four patients still have a defunctioning colostomy due to recurrence of the fistula in 2, and stenosis at the site of the bowel anastomosis in 1. The fourth patient had no complication and is awaiting colostomy closure.

Further operation to repair the 2 recurrent fistulæ was not contemplated as one had severe asthma and was on steroid therapy; the other refused operation.

At the age of 77 years, it was decided not to re-operate on the patient with stenosis.

One-Stage Group.—There were 3 post-operative deaths due to breakdown of the anastomosis in one, myocardial infarction in one and chest complications in the third. The fistula recurred in 1 patient early in the post-operative period and he required a defunctioning colostomy. The fistula healed spontaneously and the colostomy was subsequently closed.

DISCUSSION

The diagnosis of a vesico-colic fistula is straightforward in the presence of pneumaturia and fæcaluria, but on occasions only direct questioning will elicit these symptoms. Pneumaturia may be present due to gas forming organisms in the urine in the absence of a fistula, but these patients are almost invariably diabetic. The diagnosis in patients with recurrent urinary infections and no bowel symptoms is much more difficult and may only be made when the possibility of fistula formation is kept firmly in mind. In these patients the presence of a localised bladder lesion on cystoscopy is often diagnostic.

An intravenous pyelogram only serves to exclude other urinary tract abnormalities and rarely helps in the diagnosis.

A barium enema examination, however, invariably shows a bowel lesion and occasionally the fistula, but the differentiation between a carcinoma and diverticulitis of the colon is not always possible (Pugh, 1964; Lindstedt, 1967; Best and Davis, 1969).

Once the diagnosis is made, the main surgical problem is whether to excise the lesion and fistula in a one-stage operation or to give the patient a defunctioning colostomy as a first step.

The operative mortality was higher in the one-stage group, 3 out of 16, as against 1 out of 18 in the multi-stage group. This difference is even more marked if one compares 1 death in 49 major operations in the multi-stage group as against 3 deaths in 18 major operations in the one-stage group.

In comparing the two groups it became apparent that those patients with less extensive disease and in better general health had a one-stage procedure and those with a large pelvic mass had a preliminary colostomy (Table IV).

TABLE IV

Clinical Findings

	Normal	Tenderness	Mass
Multi-stage procedure	4	7	7
One-stage procedure	11	3	2

The complications of recurrent fistulæ and anastomotic stenosis in the multi-stage group could also be related to the extent of the disease, all these patients having diverticulitis. The mortality in the one-stage group should, therefore, have been lower than in the multi-stage group.

Ward *et al.* (1970) also found a higher mortality in patients treated by a one-stage procedure, whereas Couris and Block (1963) found no difference between these two groups in 21 patients, but they used "careful patient selection".

We feel that a major factor in deciding to attempt a one-stage procedure should be the ability to adequately wash out the colon above the lesion. If this cannot be done, then it is much safer to perform a preliminary defunctioning colostomy.

The long-term prognosis after treatment of a vesico-colic fistula depends on the pathology of the bowel lesion. Patients with benign disease had a good prognosis. Patients with carcinoma did not do well, all dying within two and a half years, but many had good palliation. This is contrary to the experience of Aldrete and ReMine (1967) whose series of 42 patients with carcinoma had a 5-year survival of 24 per cent and a 10-year survival of 14 per cent. They stress the value of radical surgery.

SUMMARY

A series of 68 patients with vesico-intestinal fistulæ is presented. The commonest causes were diverticulitis (58 per cent), carcinoma of the colon (19 per cent) and Crohn's disease (11 per cent).

Those patients fit enough for excisional surgery were treated by a multi-stage or one-stage

procedure. In vesico-colic fistula, the multi-stage procedure is certainly the safer procedure, but in suitable patients a one-stage operation can be safely performed, provided that the bowel can be adequately prepared.

ACKNOWLEDGEMENTS

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AGE CHANGES IN THE FEMALE URETHRA[1]

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WOMEN suffering from attacks of frequency and painful micturition, sometimes referred to as the urethral syndrome, comprise a considerable proportion of a urologist's work-load. In the Department of Urology at Southmead Hospital (Bristol) nearly 3,000 new patients were seen over a 2-year period, of whom 928 were female and of these no less than 719 were females presenting with the urethral syndrome (Table I). As part of an overall investigation into this syndrome many factors were considered including the age at which these women first experienced their symptoms. This was found to cover a wide range but if chronological age were converted to physiological or sexual age, then three distinct groups could be made (Table II). The concept of physiological age in terms of sexual activity is a valid one in the female and consists of dividing a woman's life into three phases. First there is the pre-pubertal phase, changing at the menarche to the reproductive phase, which in turn is changed by the menopause to the post-menopausal phase.

TABLE I

Incidence of Urethral Syndrome

Total patients seen over 2-year period	2,895
Total females seen over 2-year period	928
Total patients with urethral syndrome	719

TABLE II

Sexual Age At Onset of Urethral Syndrome

Sexual Age	Number of Patients with Urethral Syndrome
Pre-puberty	22
Reproductive	405
Post-menopausal	292

This physiological ageing process is under the influence of many factors, especially hormonal and in particular œstrogen activity (Marshall, 1956). Low œstrogen activity present in the pre-pubertal female, rises at the menarche to undergo cyclic variations throughout the reproductive phase in association with menstruation. Œstrogen activity rises in the early stages of the cycle to reach a peak at ovulation, after which there is a gradual decline up till menstruation (Novak and Woodruff, 1962). At the menopause there commences a gradual decline in œstrogen activity but this can vary enormously, some women maintaining adequate œstrogen levels, in the absence of a menstrual cycle, for many years (Meisel, 1966).

In some cases, however, the decline in œstrogen activity may be so severe as to result in atrophic changes in the genital tract. These are particularly marked in the vagina where they give rise to a condition known as senile vaginitis. This is characterised by an overall rigidity of the vaginal tissues with thinning, inflammation and even ulceration of the epithelium. Complete reversal of these changes can be achieved by œstrogen therapy (Midwinter, 1969).

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[1] Abridged version of the paper which received the Essay Prize of the British Association of Urological Surgeons, 1971.

Examination of the cases in the post-menopausal group shown in Table II revealed that some of these women had signs of senile vaginitis in association with their urethral syndrome. This association had been noted previously by Everett (1941), who suggested that the urinary symptoms were due to a similar process affecting the urethra, a condition he described as senile urethritis. Subsequently, Salmon and his co-workers (Salmon *et al.*, 1941) agreed with this view and pointed out the relief of symptoms obtained by treatment with œstrogens, a fact more recently confirmed by Youngblood and his co-workers (Youngblood *et al.*, 1958) and Roberts (Roberts *et al.*, 1970).

As well as this clinical correlation between urethra and vagina, there are other similarities. Firstly, both structures are alike in their anatomical structure, particularly the stratified squamous epithelium covering the distal urethra and vagina. As well as this, both structures derive, in part, a common origin from the urogenital sinus of the embryo (Langman, 1963).

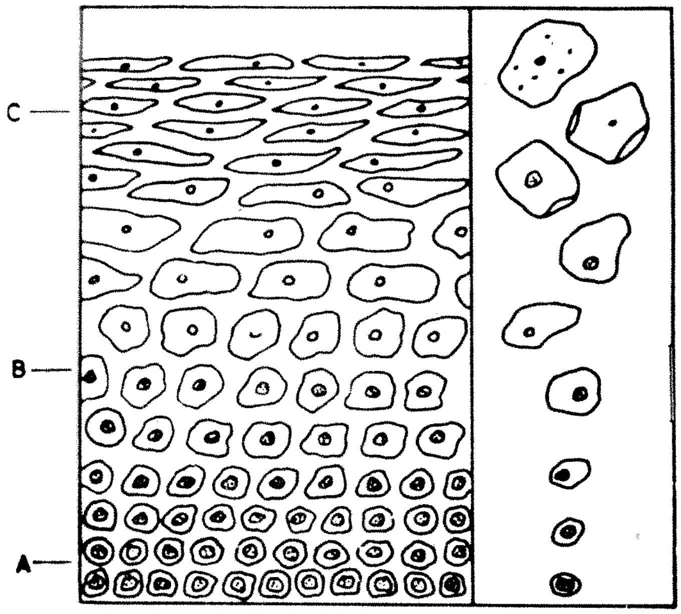


FIG. 1

Diagrammatic representation of typical squamous epithelium with the cytological appearance of the various constituents. A, Parabasal layer; B, Intermediate layer; C, Superficial layer. (The basal layer is not illustrated. Reproduced by kind permission from Wachtel, Erica G. (1964): *Exfoliative Cytology in Gynæcological Practice*, London: Butterworths.)

This close relationship between structure and development of the urethra and vagina in the female was first commented upon by Parkes and Zuckerman (1931), who noted an increase in the stratification of the squamous epithelium of the female monkey in both genital and extra-genital tissues, after the administration of large doses of œstrogen.

As a result of this and further animal experiments by Zuckerman (1936*a*, *b*, 1940) this extra-genital œstrogen sensitivity was found to be most marked in those tissues claiming origin from the urogenital sinus, and in particular the urethra. This œstrogen sensitivity was manifest by the maturation of any squamous epithelium covering these tissues.

Although the above studies were carried out on animals it seemed reasonable to assume that a similar state of affairs might exist in the human female. In this way it might be possible to show a similar œstrogen sensitivity in the human female urethra. Thus, knowing that physiological age in a woman is related to œstrogen activity, such activity could be manifest in the urethra by alterations in the maturation of the squamous epithelium covering its distal portion.

All the animal experiments mentioned previously involved histological examination of urethral tissue. Such a technique was obviously not suitable for any human experiments and some other method had to be employed to study changes in maturation of the urethral squamous epithelium.

Œstrogen activity in vaginal tissues had long been studied by a branch of cytology known as cyto-hormonal analysis. This technique was originally described in the guinea-pig by Stockard and Papanicolau (1917) and subsequently in humans by Dieks (1927) and Ramirez (1928). In 1933 Papanicolau published the classic monograph " The sexual cycle in the female as revealed by the vaginal smear " and this with later minor alteration (Papanicolau and Traut, 1943) has become the basis of vaginal cyto-hormonal analysis.

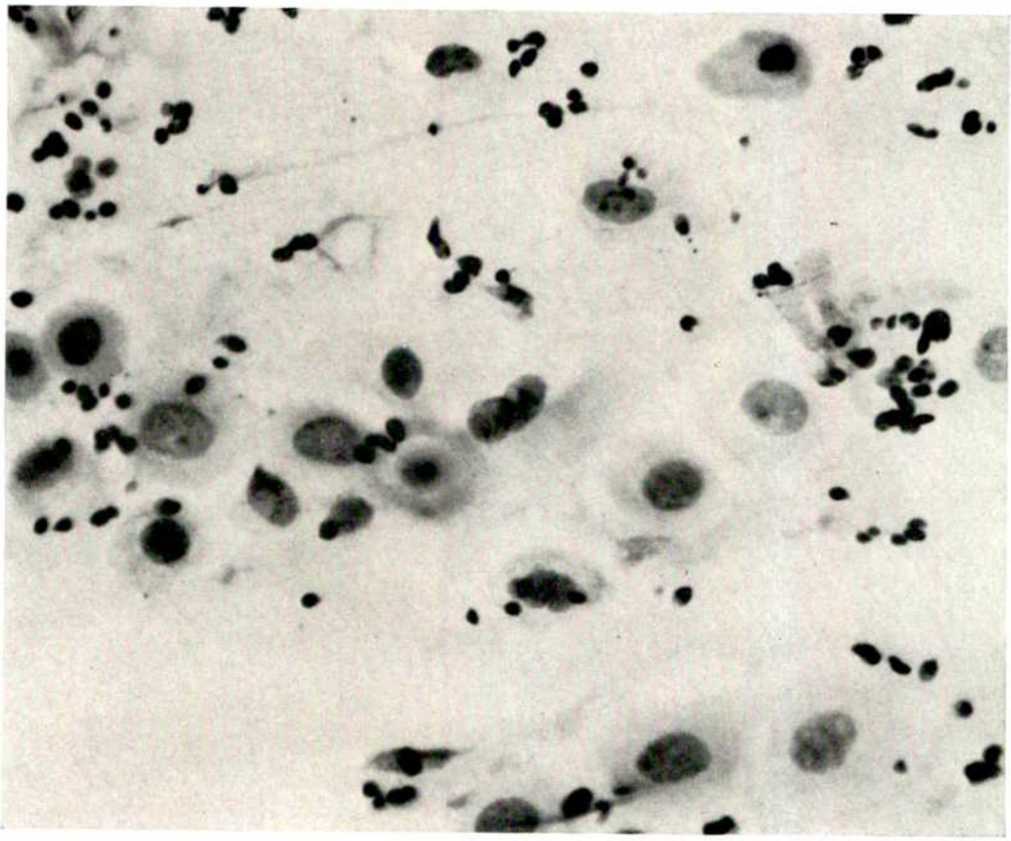


FIG. 2
Parabasal cells in vaginal smear.

The method of analysis is based on the maturation effect of œstrogen on the squamous epithelium of the vagina. When fully developed this epithelium consists of three well-defined layers derived from a basal germinal layer (Fig. 1). The first layer consists of round, plump cells with centrally placed vesicular nuclei. These are called para-basal cells. The next cell layer consists of intermediate cells which are flat and irregular with eccentrically placed vesicular nuclei. Finally, above this layer lie the superficial cells which are characteristically thin and irregular with pyknotic nuclei. The maturation of these cells from the para-basal, through the intermediate, to the superficial is dependent upon an adequate level of circulating œstrogen. Thus, by sampling the type of cell constituting the topmost layer of any vaginal epithelium (known technically as "taking a smear") it is possible to estimate the degree of œstrogen activity—the cellular pattern thus obtained reflecting an underlying tissue pattern and the biological behaviour of that tissue to œstrogen activity (Frost, 1962).

The next three figures demonstrate typical vaginal smear patterns under varying degrees of œstrogen activity. In the first (Fig. 2), the smear consists predominantly of para-basal cells indicating low œstrogen activity. In the next (Fig. 3), the cells are of the intermediate type indicating an increase in œstrogen activity, whilst the final smear (Fig. 4), shows the fully matured superficial cells confirming the presence of adequate œstrogen levels. It now remained to see if similar œstrogen changes could be demonstrated by a cyto-hormonal study of the female urethra, for if this were the case then it would be possible to demonstrate changes in the urethral squamous epithelium with differing levels of œstrogen activity. If this is then considered in terms of the normal physiological variations of such œstrogen activity occurring throughout life it could be used to support the hypothesis of ageing in the female urethra.

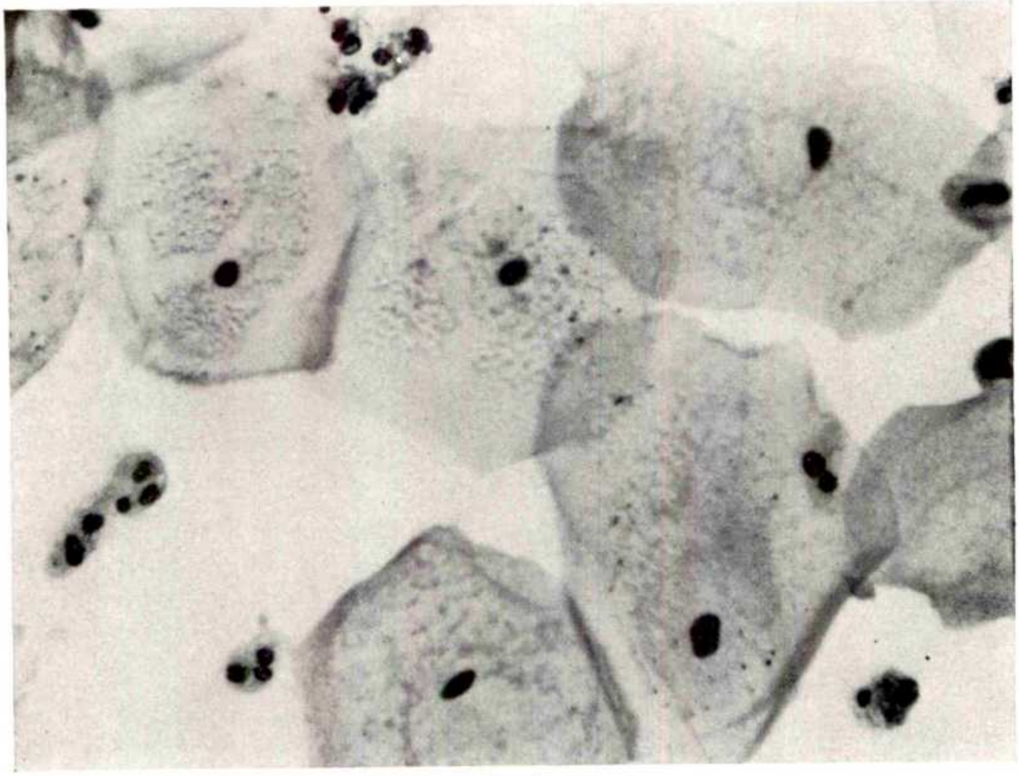


FIG. 3
Intermediate cells in vaginal smear

Once again the early references to cytology of the urinary tract are coupled with the name of Papanicolau. It was he who, together with Marshall (Papanicolau and Marshall, 1945), carried out the first systematic study of the cytology of urine. Though this work was concerned with detection of cancer in the urinary tract, subsequent papers by many authors commented on the cyto-hormonal value of urine cytology in certain physiological and clinical situations, even giving superior results than vaginal cytology in certain situations (Papanicolau *et al.*, 1948; Solomon *et al.*, 1958). Thus Biot (Biot and Beltram Munez, 1944) demonstrated the effect of ovulation on urine cytology and later McCallin *et al.* (1950) demonstrated the variations of urine cytology throughout the complete menstrual cycle, and in a later paper two of these authors correlated the same changes in the urinary sediment with endometrial histology (Stewart Taylor and McCallin, 1952). Papanicolau (Papanicolau *et al.*, 1948) reported the appearances of urine cytology with pregnancy, work later repeated and expanded by McCallin (McCallin *et al.*, 1950). Solomon (Solomon *et al.*, 1958) described changes in urine cytology in post-menopausal women treated with œstrogens and more recently work involving urine cytology has been used in the management of secondary amenorrhoea (Castellanos *et al.*, 1964), and hormone-dependant tumours (Castellanos *et al.*, 1963). Del Castillo (Del Castillo *et al.*, 1948) had earlier shown that the cells of the urinary sediment were derived exclusively from urinary tract and later in a more detailed study (Del Castillo *et al.*, 1949) concluded that the majority were derived from the distal urethra. In both these papers (Del Castillo *et al.*, 1948, 1949) the close similarity

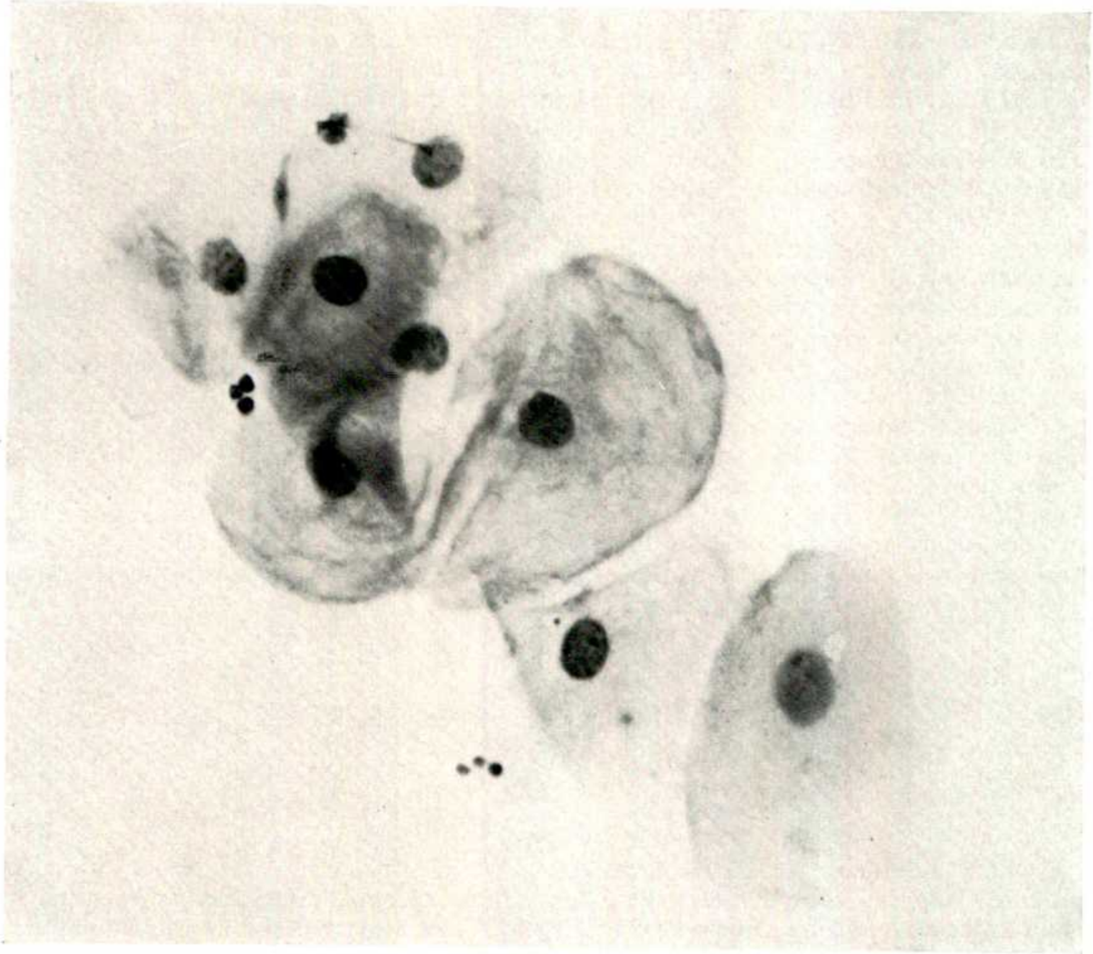


FIG. 4
Superficial cells in vaginal smear.

between urinary and vaginal smears was established, a fact subsequently confirmed in a statistical survey by Lencioni (1953).

Thus the available evidence suggested that the human female urethra was sensitive to œstrogen as shown by its cytology and that the cytological appearances were paralleled by similar changes in the vagina.

For the purposes of this work it is essential to obtain cells derived from the urethra alone. Though as mentioned above, it had been shown that the cells of the urinary sediment were mainly urethral in origin a method other than examination of urinary sediment had to be devised for accurate urethral cytology. Direct methods such as suction aspiration of the urethra were described by Papanicolau (Papanicolau *et al.*, 1945) and Del Castillo (Del Castillo *et al.*, 1949) the latter also describing, in an earlier paper (Del Castillo, 1948), urethral massage. More recently, the soluble swab technique as originally described by Kuper and his co-workers (Kuper *et al.*, 1966) has been shown to be of value in certain aspects of urethral cytology (Williams, 1968). All these methods were, however, rather complex and gave variable results in terms of cellular yield. Having regard to the success of Ayre's spatula in vaginal cytology (Ayre, 1947), a method was devised whereby a small sterilised orange stick was inserted into the distal urethra and gently rotated. The smear of cells thus obtained was spread on to one half of a glass slide, alongside a vaginal smear taken at the same time and both fixed and stained by Papanicolau's method (Papanicolau, 1942).

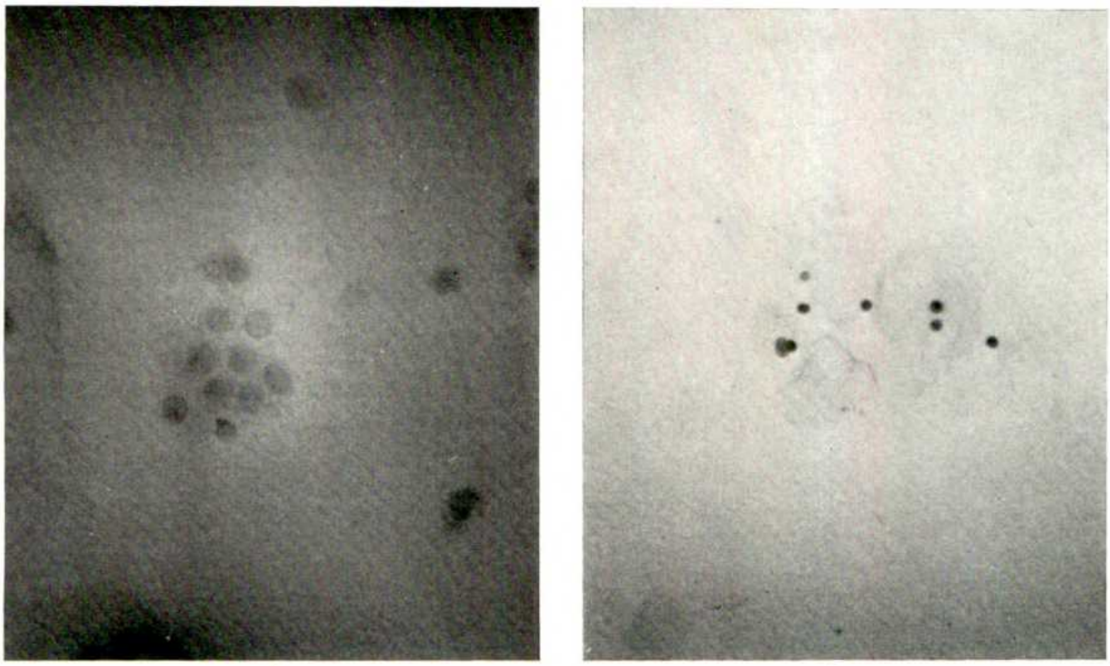
This technique was simple, cheap and effective but in view of certain ethical and practical considerations, could only be employed in those women in whom urethral instrumentation (*e.g.* cystoscopy or catheterisation) was an integral part of their treatment. Though this inevitably meant that these women were selected and hence not statistically " normal ", by excluding any factors known to interfere with cyto-hormonal analysis such as infection (Koss, 1968), drugs (Pundel, 1950; Nawab *et al.*, 1965) and previous radiotherapy (Graham, 1947) it was possible to present them as having " normal " urethræ. In this way a study of 402 females attending the Urological and Gynæcological Departments of the University of Bristol was made, the group embracing all physiological age groups (Table III).

TABLE III

Sexual Age by History of All Cases

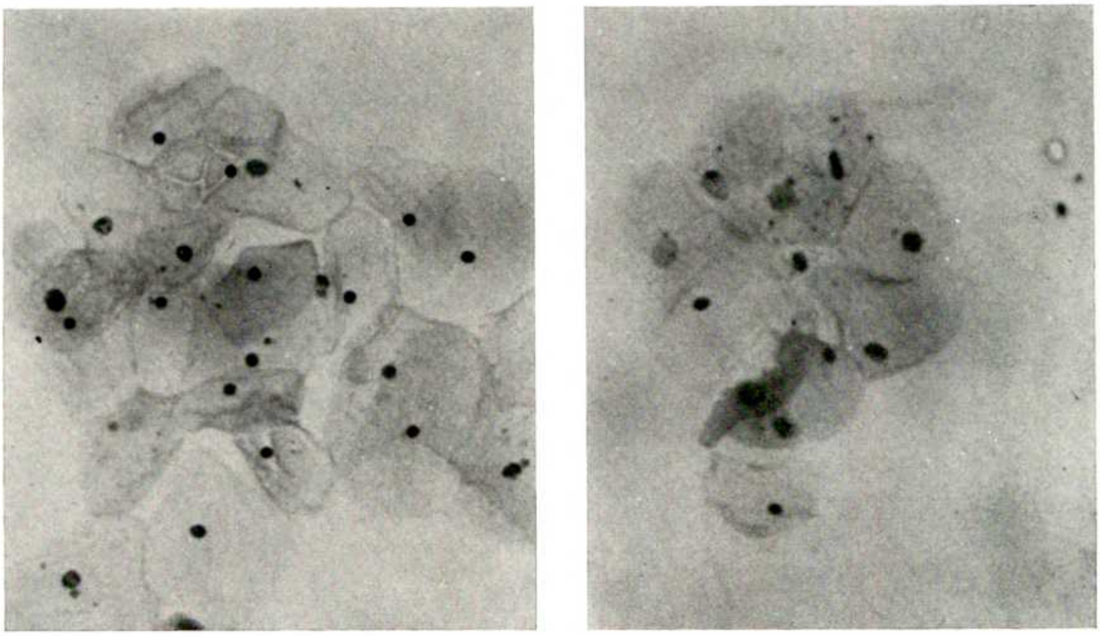
Pre-pubertal	18
Reproductive	261
Post-menopausal	123

Of the 18 children examined, 16 demonstrated typical atrophic appearances in their urethral smear indicating low œstrogen activity (Fig. 5, A). In two there was evidence of œstrogen activity in the appearance of more mature cells (Fig. 5, B). These girls commenced menstruation within 3 months of the examination, indicating that both were about to undergo the menarche when the smears were obtained. Two hundred and sixty-one women were in the reproductive phase of life and all had evidence of œstrogen activity in the urethral smear varying from the fully mature appearances associated with full œstrogen activity immediately prior to ovulating (Fig. 6, A) to the less mature smear associated with the decline in œstrogen activity in the post-ovulating phase of the cycle (Fig. 6, B). The urethral smear patterns of the 123 post-menopausal women showed three different patterns. Fifteen women had smears containing mature cells indicating the normal cyclic activity associated with full œstrogen activity (Fig. 7, A). In 85 cases there was evidence of a decline in œstrogen activity as shown by the appearance of para-basal and intermediate cells, the so-called " crowded " menopausal smear (Fig. 7, B) and finally in only 23 cases was there a true atrophic smear consisting only of para-basal urethral cells, indicating absence of œstrogen stimulation (Fig. 7, C). Thus it can be seen that in this group many women



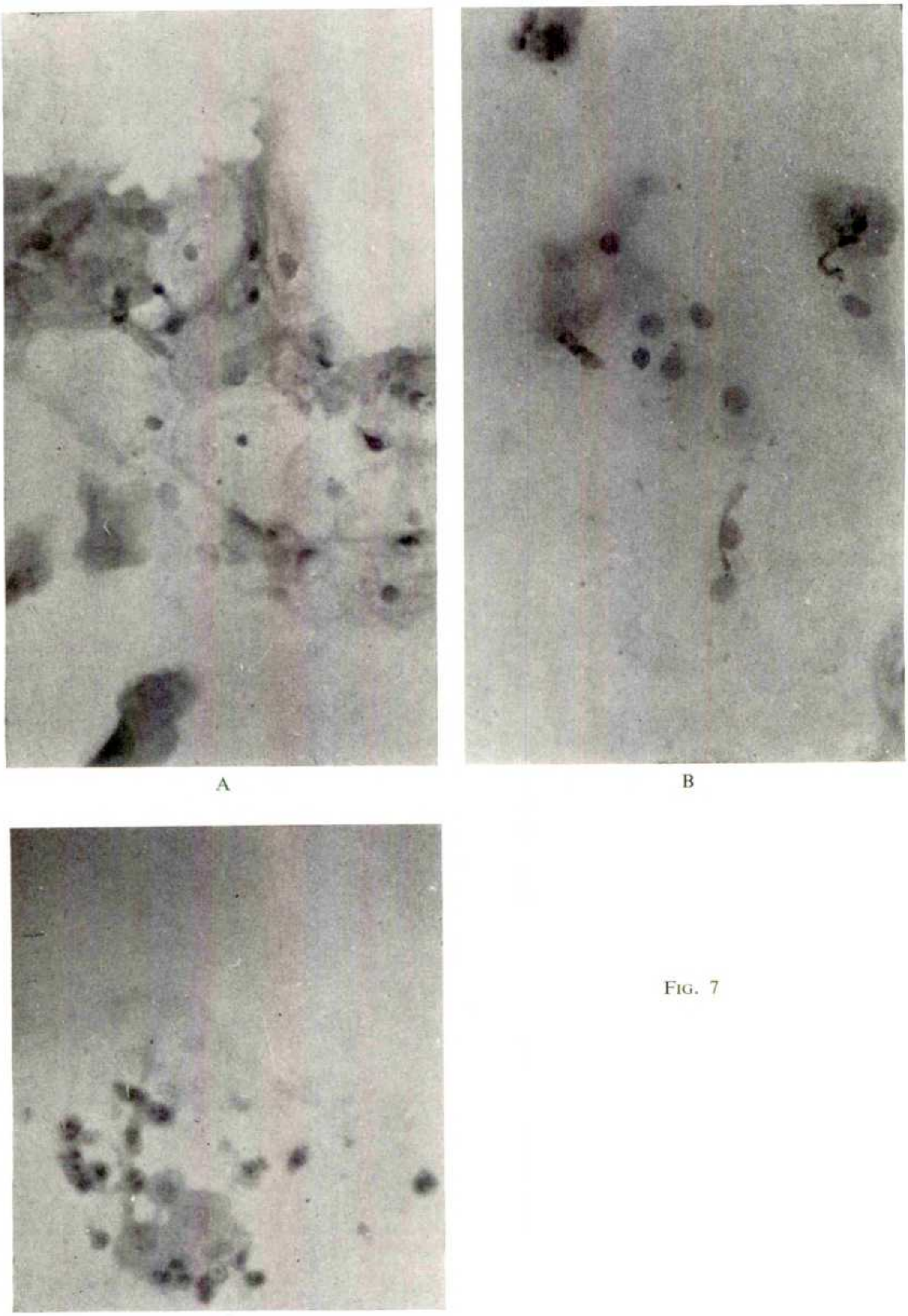
A B

FIG. 5



A B

FIG. 6



A

B

C

FIG. 7

show an œstrogen stimulated urethral epithelium up to an advanced age. This distribution of smears in post-menopausal women indicating varying levels of œstrogen activity is in accordance with the post-menopausal vaginal cyto-hormonal studies of Stoll (1960) and Meisel (1966) and demonstrates that abrupt atrophic changes in the urethra do not necessarily follow at the onset of the menopause. In all the cases studied the vaginal cells mirrored those of the urethral smear and showed the same variation under the differing œstrogen environments associated with the various age-groups.

These results confirm that there is a natural ageing process in the female urethra related to physiological variations in œstrogen activity and thus provides a basis for the diagnosis and treatment of atrophic senile urethritis.

This work was mainly carried out whilst working in the Urology Department at South Mead Hospital, Bristol and was completed during my present appointment as Senior Registrar in Urology at Leeds and Bradford. I would like to express my thanks to all the medical and nursing staff of both departments for their endless help and encouragement in this work and particularly to Mr Michael Roberts, Consultant Surgeon, Bristol Royal Infirmary, for his personal interest and enthusiasm.

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A QUANTITATIVE INVESTIGATION OF THE EFFECTS ON THE GROWTH OF CALCIUM OXALATE CRYSTALS ON POTENTIAL INHIBITORS

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Calcium oxalate is one of the most common constitutents of renal calculi. The presence of this compound in the nucleus of most calcium-containing stones and the discovery by Hodgkinson (1969) that the smaller the stone the greater the proportion of calcium oxalate, have encouraged the idea that calcium oxalate may be an important factor in the initiation of renal stones. As calcium oxalate crystals are easily produced *in vitro*, a number of investigators have designed experiments to study the formation of these crystals and the effect of various substances on their growth rate. Lyon and Vermeulen (1965) grew oxalate crystals on wire loops suspended in water or a simple salt solution by the slow diffusion of calcium and oxalate ions through filter paper wicks into the media. Some compounds, considered to be potential inhibitors of crystal growth, were added to the media and the crystals examined after a number of days. Using a similar method, Sutor (1969) examined the effects on calcium oxalate growth of a wide variety of substances using an acetate buffer. A further paper by Sutor and Wooley (1970) examined the action of other compounds in the acetate buffer and also in human urine. In all these experiments the crystals were allowed to grow for approximately 1 week and then studied by simple observation. However, this method of assessment is subjective and not in any way quantitative. In this paper, a method is described for the estimation of crystal growth by measuring the calcium content of crystals. Substances which might be expected to inhibit calcium oxalate growth were added to acetate buffer and human urine. Their effects on the formation of crystals over a 24-hour period were studied.

Experimental.—The technique used for calcium oxalate growth was similar to that of Sutor (1969). The medium, consisting of either 0·2 molar acetate buffer, pH 6·4, or human urine from a bulk collection adjusted to a pH 6·4, was placed in a 100-ml. beaker. The calcium and oxalate ions from solutions of 0·1 molar calcium chloride and 0·1 molar sodium oxalate respectively were allowed to diffuse into the medium via Whatman No. 4 filter paper wicks, for 24 hours. Crystals formed on glass threads which were suspended in the medium to a depth of approximately 20 mm. All experiments were carried out at room temperature, approximately 20°C. In order to obtain an accurate assessment of the growth rate, two glass threads were suspended in each of six separate beakers. After the 24-hour period, the exact depth of each thread in the medium was measured, and the calcium oxalate deposit dissolved in 4 ml. of 0·25 N hydrochloric acid. The solutions were analysed for their calcium content using a Technicon Auto-Analyser. A modification of the Technicon Methodology N-3b was used for this assay. By eliminating dialysis and increasing the sample volume it was possible to measure concentrations of calcium as low as 0·2 mg. per 100 ml. The twelve values obtained for each experiment were calculated for a depth of 20 mm. in the medium.

RESULTS

The method described for calcium oxalate growth was studied using the acetate buffer in order to determine the best conditions for investigating the inhibiting effect of added compounds. Twelve glass threads were immersed in the media to a depth of approximately 20 mm. for periods of 8, 16 and 24 hours. The average calcium concentration for the threads were 0·4, 1·3 and 2·7 mg. per 100 ml. respectively. From these findings it was decided that adequate crystal growth occurred in 24 hours.

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Glass threads were immersed at depths of 10, 15, 20 and 25 mm. and the average calcium content of the crystals were found to be 1·4, 1·9, 2·0 and 3·5 respectively. These results indicate a reasonable linear increase in crystal deposition with increasing depths of immersion, which justified the correction of all results to a standard depth of 20 mm. The reproducibility of the method was studied by growing eight batches of twelve threads in buffer and calculating the standard deviations. The in-batch standard deviation was 18·4 per cent of the mean and the between-batch standard deviation, 3·2 per cent of the mean. The high in-batch standard deviation confirmed the need to perform twelve procedures in each batch to ensure reproducible results. Calcium oxalate crystals were grown in urine and acetate buffer at pH values of 5, 6, 7 and 8. As no significant changes in growth rates were observed it was considered that moderate variations in pH did not have an appreciable effect on the formation of these crystals.

TABLE I

Results of the Effects on Calcium Oxalate Growth in Acetate Buffer and Urine at pH 6·4 by Metallic Ions

Concentrations of Metallic ions		Compound Added to Medium	% Growth Relative to Control	
			Buffer	Urine
Sodium	100 mEq./l.	Sodium chloride	52	148
	200 mEq./l.	Sodium chloride	83	177
	400 mEq./l.	Sodium chloride	110	153
Potassium	50 mEq./l.	Potassium chloride	140	166
	100 mEq./l.	Potassium chloride	103	136
	200 mEq./l.	Potassium chloride	112	169
Lithium	25 mEq./l.	Lithium carbonate	87	87
	50 mEq./l.	Lithium carbonate	86	62
	100 mEq./l.	Lithium carbonate	76	56
Magnesium	125 mg./l.	Magnesium chloride	110	74
	250 mg./l.	Magnesium chloride	116	117
	500 mg./l.	Magnesium chloride	100	120
Zinc	125 mg./l.	Zinc chloride	42	144
	250 mg./l.	Zinc chloride	42	166
	500 mg./l.	Zinc chloride	11	132
Aluminium	20 mg./l.	Aluminium chloride	46	105
	40 mg./l.	Aluminium chloride	15	118
	80 mg./l.	Aluminium chloride	12	109

A number of selected compounds were added to the acetate buffer and the urine, the solutions were adjusted to a pH of 6·4 and the amount of calcium oxalate forming on the glass fibres was determined as previously described. As a control the crystal growth in the appropriate medium was estimated in each experiment. The relative growth rates in the presence of each added compound were calculated as percentages of the average value obtained in the control medium. Values below 50 per cent indicate inhibition and above 150 per cent suggest accelerated growth.

The monovalent ions, sodium and potassium, stimulate growth in urine but have no effect

TABLE II

Results of the Effects on Calcium Oxalate Growth in Acetate Buffer and Urine at pH 6·4 by Miscellaneous Compounds

Concentration of Compound Added to Medium		% Growth Relative to Control	
		Buffer	Urine
Pyrophosphate (sodium salt)	75 mg. P/l.	80	72
	150 mg. P/l.	66	55
	300 mg. P/l.	14	19
Urea	12·5 g./l.	64	70
	25 g./l.	96	110
	50 g./l.	83	71
Ascorbic Acid	2 g./l.	97	110
	4 g./l.	177	120
	8 g./l.	114	130
Salicylic Acid	1 g./l.	102	83
	2 g./l.	80	108
	4 g./l.	113	83
Citric Acid	2 g./l.	46	100
	4 g./l.	18	91
	8 g./l.	5	54
Amino Acid mixture	2·5 g./l.	66	103
	5 g./l.	77	92
	10 g./l.	58	99
Tetracycline	250 mg./l.	59	120
	500 mg./l.	49	80
	1·0 g./l.	—	40
Teepol	0·05 ml./l.	62	91
	0·1 ml./l.	49	41
	0·2 ml./l.	5	42

TABLE III

Results of the Effects on Calcium Oxalate Growth in Acetate Buffer and Urine at pH 6·4 by Dyestuffs

Dyes Added to Medium		% Growth Relative to Control	
		Buffer	Urine
Methylene blue	5 g./l.	7	97
Malachite green	5 g./l.	0	18
Methyl violet	5 g./l.	30	105
Nigrosine	5 g./l.	0	112
Eosin	5 g./l.	22	106
Hæmatoxylin	5 g./l.	62	81

in buffer, while lithium shows some inhibitory effects at relatively high concentrations in buffer and urine. Magnesium ions appear to have no inhibiting effect, in spite of many reports indicating that reduced output of magnesium may be one of the causes of renal calculi. Zinc and aluminium ions were effective inhibitors in acetate buffer but had no effect in urine. Sutor and Wooley (1970) observed inhibition in urine by both these ions. The results for these metals are shown in Table I.

Pyrophosphate, in relatively large concentrations, inhibited growth in buffer and urine (Table II), however, it is very doubtful if there is any inhibitory effect in the quantities occurring in urine as have been suggested by Russell and Fleisch (1969).

The values for the following miscellaneous substances are given in Table II. Compounds such as urea, ascorbic acid and salicylic acid did not effect crystal growth in either buffer or urine while sodium citrate and amino-acids reduced growth in buffer only. Tetracycline was an effective inhibitor in buffer and to a limited extent in urine. Teepol was found to be a most effective inhibitor of crystal growth in both buffer and urine.

The large number of dyes tested by Sutor (1969) in acetate buffer medium inhibited the growth of calcium oxalate crystals. Six dyes, listed in Table III, were added to the buffer and urine at a concentration of 5 g. per litre. In the buffer medium all the dyes retarded crystal growth but in urine only malachite green produced any inhibition.

CONCLUSION

The method described for the quantitative estimation of calcium oxalate growth and the action of potential inhibitors appears to be reasonably accurate and reproducible. Many substances which were potent inhibitors of crystal growth in the buffer were found to be inactive in a urine medium. Investigations of renal calculi formation involving *in-vitro* studies of calcium oxalate growth should be performed in urine only, as synthetic media may produce irrelevant and misleading results. The inhibitory effects in urine of Teepol, tetracycline, pyrophosphate and malachite green are of considerable interest.

SUMMARY

The technique for the growth of calcium oxalate crystals by the slow addition of calcium and oxalate ions to a medium was standardised. A quantitative method of assessing crystal growth was developed by estimating the calcium content of the crystals using a modified Auto-Analyser procedure. Various substances were added to a buffer medium and human urine in order to study their effects on the growth of calcium oxalate crystals. Contrary to findings by other workers many of the compounds which were effective inhibitors in the buffer medium did not suppress crystal growth in human urine. Malachite green, sodium pyrophosphate and to a lesser extent tetracycline and Teepol were among the few effective inhibitors in both urine and buffer medium.

We wish to thank Mr H. McCambridge for his technical assistance with this work.

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HÆMATURIA AND RENAL FORNICAL LESIONS

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RENAL bleeding due to small lesions of the renal papilla or fornix has been described under a variety of terms such as hæmorrhagic papillitis (McKay *et al.*, 1949), varices of the renal papillæ (Webb-Johnson and Warwick, 1941; Bobbitt *et al.*, 1944), focal hæmorrhagic pyelonephritis (Wilbur and Priestley, 1935), renal fornical hæmorrhage (Pytel, 1960), pyelo-venous fistula (MacMahon and Latorraca, 1954; Meservey and Scordamaglia, 1956), palindromic unilateral renal purpura (Nation *et al.*, 1952) and focal renal papillary necrosis (Pearman and Beach, 1962). Somerset and Harkness (1960) discussed the pathological findings of 7 cases of hæmaturia of obscure origin and described vascular and degenerative changes of the sub-epithelial tissue of the pelvis and calyces but made no attempt to define their observations in terms of diagnosis.

These conditions occur infrequently and are difficult to delineate because of their size and position. Pytel (1960) hinted that many of these lesions were related and Pearman and Beach regarded them as " relative degrees of perhaps a somewhat analogous condition ". Disturbances of vasculature of papillæ and venous fornical plexuses form the common denominator of all the conditions. The first histological demonstration of a direct channel of communication between the lumen of a dilated venous sinus and an adjoining calyx (MacMahon and Latorraca, 1954) was a chance finding. Demonstration of most other lesions has resulted from serial or multiple sections of papillæ which have been congested, hæmorrhagic or associated with adherent clot. Pearman and Beach recognised the need for examination of the fresh specimen with a magnifying glass by a pathologist so that tissue blocks of suspicious areas could be selected and orientated and multiple serial or step sections studied.

Clinically these patients present a difficult problem of management. They suffer from hæmaturia, either persistent or recurrent, for which no cause can be found and which may not respond to conservative therapy. Nephrectomy has to be performed in many of these cases but more conservative renal surgery, usually partial nephrectomy, is possible in some (Pytel, 1970).

In this paper we report 3 cases of hæmaturia due to lesions of the renal fornix, comment on examination of the kidney, and describe the pathological changes found in sections of 200 unselected renal fornices taken from our autopsy records. Based on the result of this study we discuss a possible pathogenesis of some of these cases.

CASE REPORTS

Case 1.—A 27-year-old Caucasian mother of five children presented with continuous hæmaturia of 7 weeks' duration. She suffered from a moderate degree of familial deafness and had had hepatitis at the age of 8 years. Physical examination was normal. The hæmoglobin was 13·3 g. per cent falling to 11·6 g. per cent over 2 weeks, white blood cells 10,000/c.mm. with slight polymorphonuclear leucocytosis, and E.S.R. 24 mm. in 1 hour (Westergren). Biochemical tests of renal function were normal and there was no evidence of a blood coagulation defect. Cystoscopy showed a normal bladder with bloody efflux from the left ureter. Radiological studies which included intravenous pyelography, retrograde pyelography, aortogram and left selective renal angiogram were all normal. A renal biopsy showed no abnormality. The gross hæmaturia continued and the hæmoglobin fell to 7·9 g. per cent 3 weeks after admission. She was transfused with 4 pints of whole blood. The bleeding continued and after further cystoscopy had confirmed the left side as its source, nephroureterectomy was carried out. The post-operative course was uneventful. Hæmaturia ceased and there had been no recurrence 1 year after operation.

Pathological Findings.—*Macroscopic.*—The left kidney measured 11 × 4·5 × 3 cm. and on the postero-lateral aspect there was a small hæmatoma from the renal biopsy measuring 3 × 2 × 0·5 cm. The external surface of the kidney was smooth. The hemisected surfaces were unremarkable but there was blood-stained urine in the pelvis and ureter with a small clot in the lower polar calyx. Dissecting microscope examination showed small hæmorrhagic areas in the fornix of the lower polar calyx.

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Microscopic.—Sections of carefully selected blocks of the hæmorrhagic areas showed recent submucosal hæmorrhages except for one lesion. This appeared as a " micro-diverticulum " of the calyx at the fornix. It was lined by epithelium at its neck but otherwise the epithelium had been denuded except for two areas where occasional lining cells remained attached. The micro-diverticulum which contained clot and desquamated epithelium was in direct contact and communication with thin-walled blood sinuses, and was surrounded by small hæmorrhages (Fig. 1).

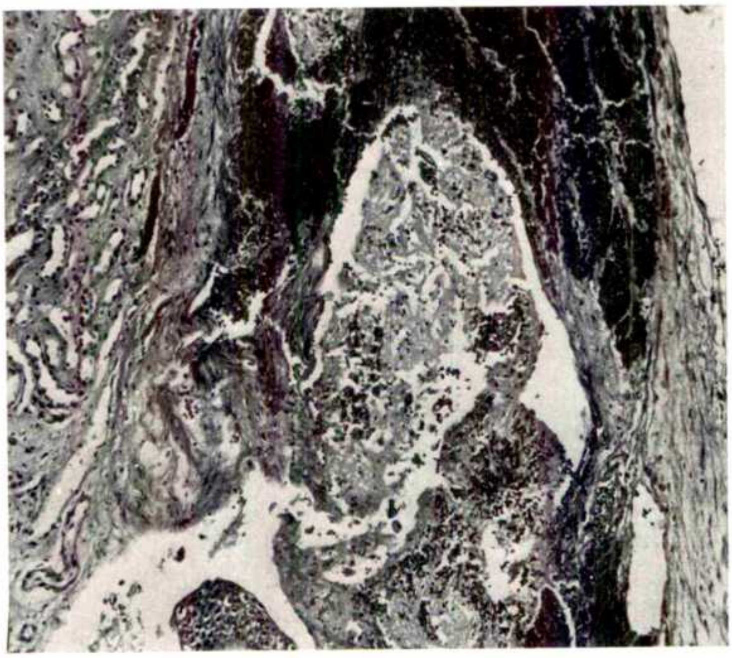

FIG. 1

Photomicrograph of the veno-calyceal fistula in case 1. A " microdiverticulum " at the renal fornix containing clot and desquamated epithelium is in direct contact and communication with thin-walled blood sinuses and is surrounded by small hæmorrhages. (H. & E. × 104.)

It was concluded that a veno-calyceal fistula was present, consisting of thin-walled sinuses leaking into a sub-epithelial space in turn opening into the calyx at the fornix.

Case 2.—A 60-year-old Caucasian woman presented with continuous hæmaturia of 3 months' duration. There were no other symptoms. She had had an attack of " pyelitis " as a young woman and a brief period of hæmaturia of unknown cause 10 years previously which had settled spontaneously. Physical examination was normal. Hæmatological and biochemical investigations were essentially normal. Urine analysis showed protein +, many red blood cells, and 4 to 8 white blood cells per high power field. No casts were seen and no growth occurred on culture. An intravenous pyelogram was normal. Cystoscopy showed a normal bladder with blood coming from the right ureteric orifice. A right retrograde pyelogram was normal as was a subsequent aortogram and selective right renal angiogram. Because hæmaturia persisted, a right nephrouretectomy was performed after a cystoscopy had verified right-sided bleeding. The patient made an uneventful recovery and at follow-up 3½ months later there had been no recurrence of bleeding.

Pathological Findings.—*Macroscopic.*—The right kidney weighed 154 g. and measured 11 cm. in length. The capsule stripped leaving a fairly smooth surface. The hemisected surfaces showed normal cortex and medulla. One papilla at the lower pole was congested with hæmorrhage at the fornix.

Microscopic.—Examination of multiple blocks of the congested pyramid showed a microscopic epithelial-lined cyst in the upper papilla which opened into the calyx at the fornix. Capillaries in the outer part of the papilla were telangiectatic and there were dilated capillaries with small hæmorrhages in the renal sinus connective tissue. That part of the calyceal mucosa forming one arch of the fornix was corrugated in appearance and contained an opening into a partially epithelialised cystic space in the sub-epithelial connective tissue. A small vein opened directly into the latter cavity and there was mild chronic inflammatory cell infiltration in surrounding tissue (Fig. 2). The epithelium lining the fornix was unusual in that there were patchy areas of proliferation of cells showing atrophic features in that they were smaller than normal with dark nuclei and little cytoplasm.

It was concluded that a veno-calyceal fistula was present in the form of a venous channel opening into a submucosal cavity in turn opening into the calyx. The telangiectatic vessels in the tissue of the papilla forming the outer cyst wall were considered to be only a potential source of bleeding.

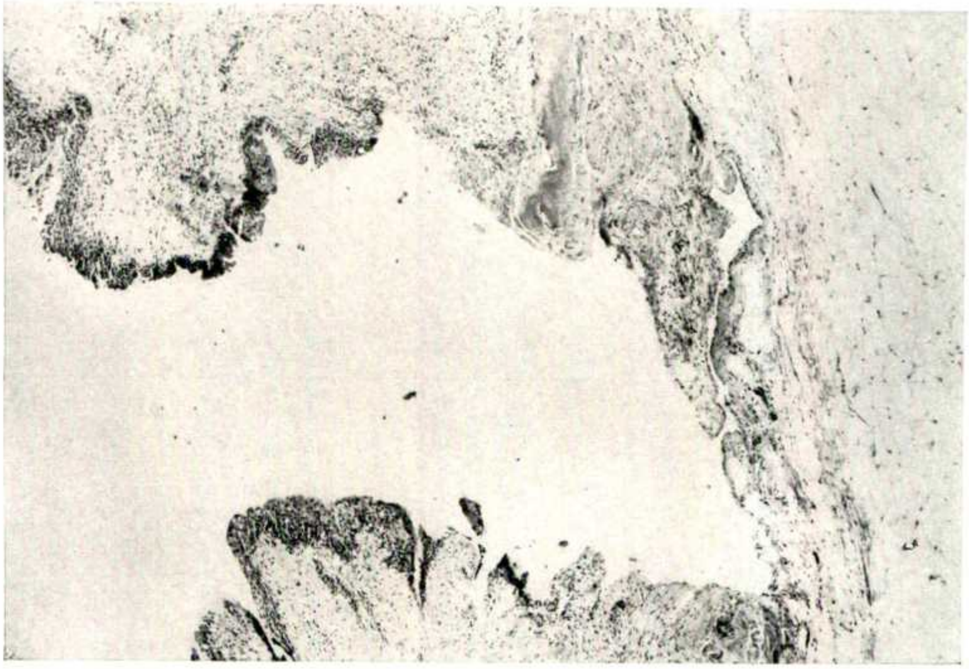

FIG. 2

Photomicrograph of the veno-calyceal fistula in case 2. A partly epithelialised "micro-diverticulum" at the renal fornix is in direct communication with a vein. (H. & E. × 37.)

Case 3.—A tall 29-year-old Caucasian woman presented with gross painless hæmaturia of 2 weeks' duration associated with intermittent slight dull ache in the right loin. She had suffered from 3 episodes of frequency and pain on micturition 1, 2 and 3 years previously and had been taking up to 5 A.P.C. powders a day for 6 years because of neck pain and headaches after an injury of the cervical spine. Physical examination was normal as were all hæmatological studies and biochemical tests of renal function. Urinalysis showed many red cells, 6 to 8 white cells per high power field, no casts and a small amount of protein. No growth was obtained on culture. An intravenous pyelogram showed enlarged kidneys (left 16·8 cm., right 15·5 cm.) of normal shape and position. The left pelvicalyceal system was normal but on the right side there was an irregular filling defect 15 × 5 mm. related to a papilla of the uppermost calyx (Fig. 3). This was diagnosed as either blood clot or papillary neoplasm.

Cystoscopy showed a normal bladder and bloody efflux from the right ureter. A right retrograde pyelogram demonstrated a pelvic filling defect consistent with blood clot and the persistence of the defect in the upper calyx. A subsequent aortogram and selective renal angiogram were normal. Urinary cytology did not show malignant cells. She was treated conservatively for 2 months but the bleeding did not stop and she became tired and listless. Cystoscopy reaffirmed that the bleeding was right sided and it was decided to perform an upper polar nephrectomy and to examine the specimen in the operating theatre. This was done and the pathologist was able to give reasonable assurance that a veno-calyceal fistula had been found and that no tumour was present. The surgeon, therefore, did not proceed to nephroureterectomy but closed the wound. There was no hæmaturia post-operatively, but minor chest and urinary infections had to be treated. Hæmaturia had not recurred at the 6 months follow-up period and the check intravenous pyelogram showed normal appearance apart from the absence of the upper pole of the right kidney.

Pathological Findings.—*Macroscopic.*—The upper pole of the right kidney measured 5 × 6 × 3 cm. The upper polar calyx was slightly dilated and contained clot. The hemisected surfaces showed congestion of the papilla. Dissecting microscope examination of the fornix showed a pit-like hæmorrhagic lesion.

Microscopic.—Serial sections of the chosen area showed an epithelial-lined cavity in the papilla of microscopic dimensions which opened into the calyx at the fornix. This cavity had fistulous communications with small capillary structures which were partly epithelialised (Figs. 4 and 5). The outer papilla which formed the wall of the cavity showed telangiectasia of the capillary vasculature. Small recent submucosal hæmorrhages were present in the calyceal mucosa, and as well there was a lesion consisting of a partly epithelialised submucosal cavity opening into the calyx and lying adjacent to a vein.

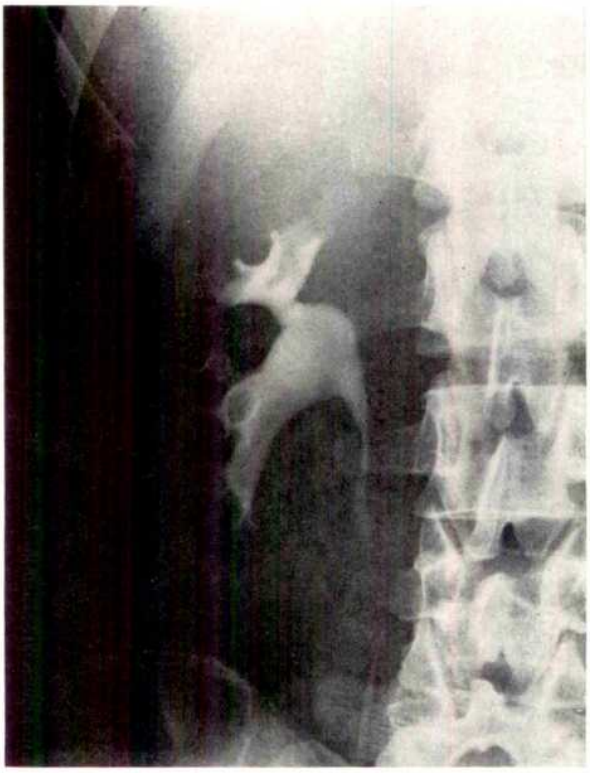

FIG. 3

Intravenous pyelogram, case 3, showing the persistent filling defects of the most medial upper calyx of the right kidney.

It was concluded that one definite veno-calyceal fistula had been demonstrated consisting of partly epithelialised capillaries opening into a cyst of the papilla which in turn opened into the calyx and that a second potential if not actual veno-calyceal fistula was present taking the form of a partly epithelialised submucosal cavity opening into the calyx and either directly adjacent to or communicating with a vein. The telangiectatic capillary vasculature of the outer papilla was considered a potential source of bleeding only.

HISTOPATHOLOGICAL STUDY OF RENAL FORNICES

Routine autopsy examinations in the Department of Pathology, Royal Perth Hospital, Western Australia, have included a section of the kidneys through the tip of a papilla. Most sections, therefore, show the fornix and adjacent tissue. An unselected consecutive series of slides of kidney in which the fornix could be studied were taken from the autopsy files and abnormalities scored in 200 cases. All slides examined in the first instance were hæmatoxylin and eosin stained 5μ paraffin sections. Where necessary, appropriate special stains were used.

In scoring, the term indolent inflammation was used to describe an abnormality consisting of infiltrations of lymphocytes, mast cells, occasional vesicular histiocytes and fibroblasts in the renal sinus tissues as distinct from an active inflammatory infiltration consisting of lymphocytes, plasma cells, polymorphs and granulation tissue. Connective tissue cystic change was used to describe spaces in the renal sinus connective tissue. Some were epithelialised, many were not, and in a number the epithelium was desquamated and showed hydropic change. Terms used to describe other abnormalities are readily understandable. The results are listed in the Table.

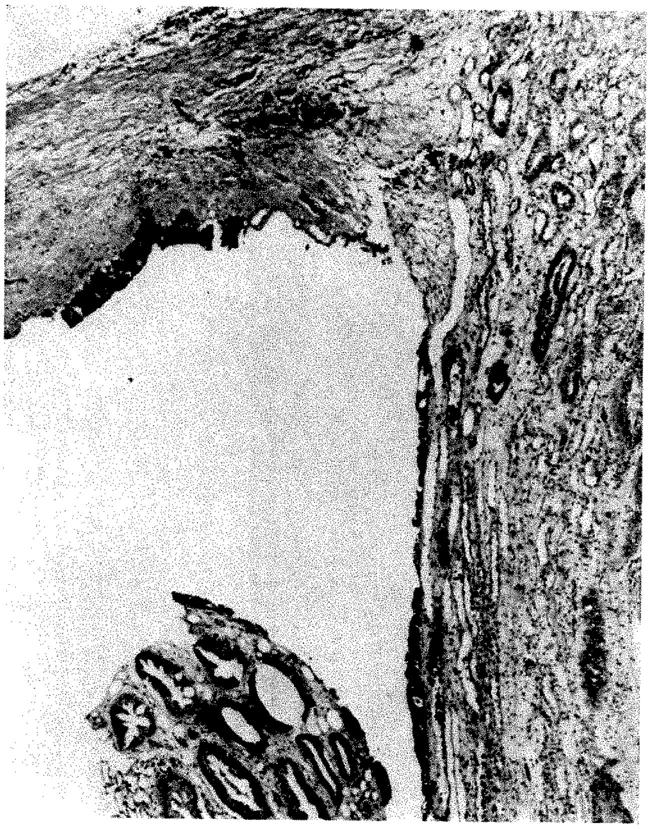

FIG. 4

Photomicrograph of the lesion in case 3 showing a cyst in the upper papilla with a wide opening into the calyx. One of the several partly epithelialised fistulous communications with capillary structures is at the fornix. A degree of capillary telangiectasia is evident on the lateral aspect of the papilla. (H. & E. × 37.)

DISCUSSION

The demonstration of vascular channels directly communicating with the calycine cavity was a result of an awareness of these lesions and a planned method of examination of the kidney to find them. We have found that the fresh kidney specimen must be carefully hemisected and examined at once because, after fixation, the fornix cannot be adequately visualised without tearing either papilla or the tissues of the wall of the calyx. In the fresh state the tissues are soft and pliable and the arches of the fornix can be gently separated with blunt probes so that the fornix can be assessed with a dissecting microscope. The lesions that we have observed by

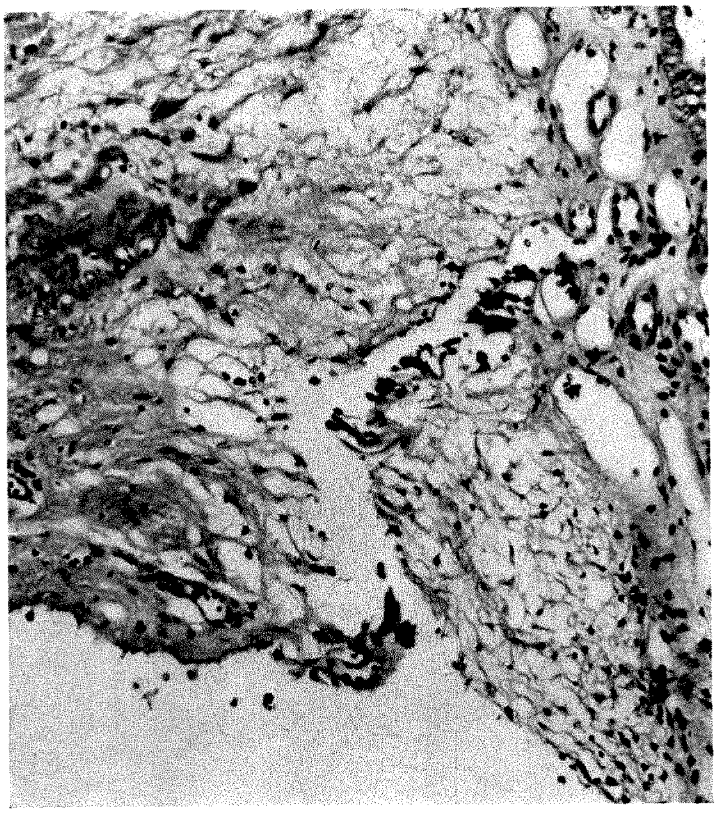

FIG. 5

Photomicrograph showing the partly epithelialised fistulous communication with capillary structures depicted in Fig. 4. (H. & E. × 170.)

TABLE

Histological Observations on an Unselected Series of Renal Fornices

Number of Cases Examined = 200

Type of Change	Number
Normal	26
Inflammation—Active chronic	6
—indolent	77
Œdema	82
Fibromuscular hypertrophy of wall of calyx	44
Fibrosis of wall of calyx	44
Connective tissue microcystic change	65
Connective tissue hæmorrhages	25
Iron pigment deposition	17
Vascular telangiectasia	6
Micro-diverticulum of calycine mucosa	6
Cell nests of von Brunn	23
Metastatic tumour	3

this method have been focal hæmorrhages, " pits ", or separation of the mucosa lining the calyx from the mucosa lining the papilla. The exact bleeding point has not been identified in this way, but the examination does show areas of abnormality at the fornix. If these are noted, after suitable fixation, blocks of tissue can be taken and orientated according to the now known areas of abnormality at the fornix. Then multiple, step, or serial sections can be made and studied.

This technique was used in cases 1 and 3 to demonstrate the lesions, but the lesion in case 2 was found after examination of multiple blocks of a papilla where fornical hæmorrhage could be seen macroscopically on the hemisected surface.

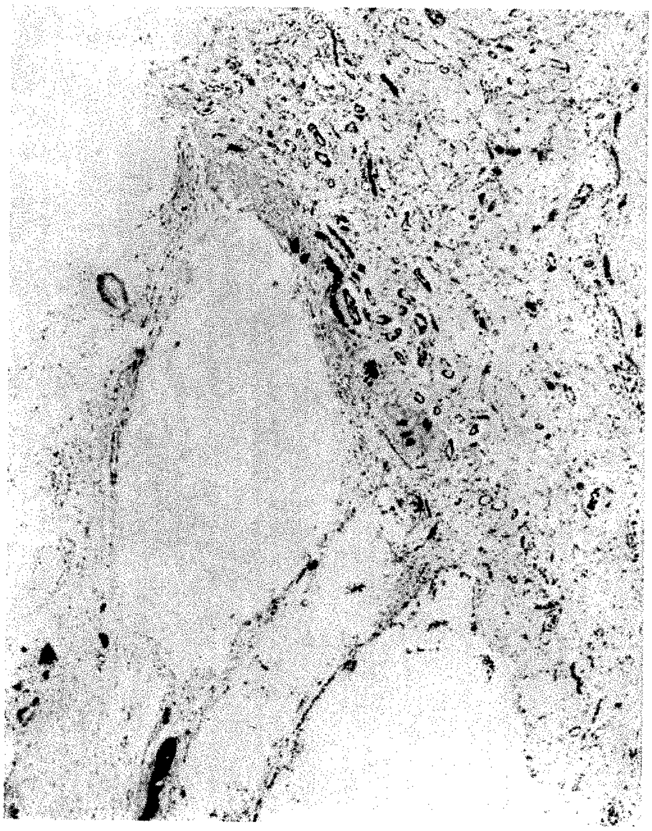

FIG. 6

Photomicrograph showing microcystic change in the renal sinus connective tissue. Over 30 per cent of renal fornices show varying degrees of this change. (H. & E. × 37.)

In case 3 partial nephrectomy was performed because of a persistent pyelographic abnormality, and immediate examination of the fresh specimen with the dissecting microscope in the operating theatre suggested a significant renal fornical lesion was present. Pytel (1970) also performed partial nephrectomy in 11 of his 16 cases, but his surgical approach was determined solely by pyelographic demonstration of a veno-calyceal canal. Whilst it is true that in the context of a patient with obscure renal bleeding showing a horn abnormality in the pyelogram, the abnormality is almost certainly a venous calyceal canal, it is also possible that the horn is a pyelosinus or pyelolymphatic canal. A partial nephrectomy which removes one of these latter lesions will not cure hæmaturia due to an open veno-calyceal canal situated elsewhere in the kidney. Dissecting microscope examination of these specimens could also give false-positive information because the " pits " and splits observed at a fornix could as well be pyelo-sinus or pyelolymphatic lesions as veno-calyceal canals. If however the " pit " is associated with overlying blood clot then its chances of being a pyelo-sinus or pyelolymphatic lesion are considerably reduced.

The morphological lesions in our cases have strikingly similar features in that a vessel opened into a small sub-epithelial cavity which in turn opened into the calyx. An identical lesion is depicted in Fig. 5 by Pytel (1960). This suggested a common pathogenesis in that sub-epithelial cystic change may be a fundamental lesion in the development of venous calyceal canals.

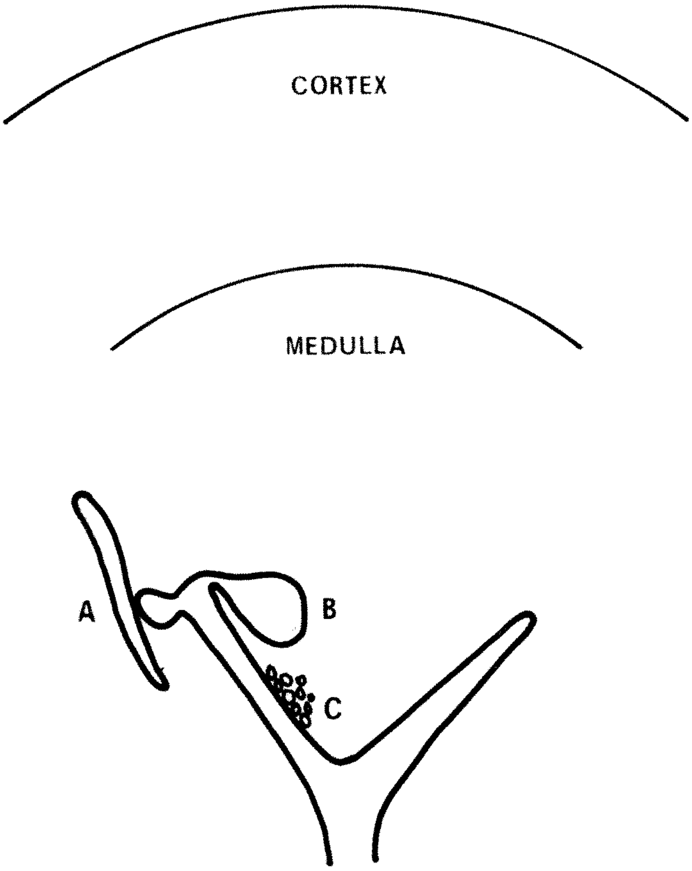

FIG. 7
Diagrammatic representation of the topographical similarity of the lesions. A represents the microcystic change in the renal sinus connective tissue adjacent to venous sinuses and present in each case. B, depicts the cystic change in the upper papilla, and C, the vascular telangiectasia in the outer papilla. These latter two changes were present in cases 2 and 3.

The results of the morphological study of unselected renal fornices given in Table I show that only 13 per cent of renal fornices were normal. The remainder showed one or several histological abnormalities. The most common change was a combination of fibrosis, œdema, fibro-muscular hypertrophy, and lymphocyte and mast cell infiltrations (about 40 per cent). Sub-epithelial cystic change occurred in 30 per cent (Fig. 6). These appearances may well be the morphological changes that result from urine infiltration into the renal sinus connective tissue which, according to Pytel (1970) is due to pelvi-calyceal hypertension and dyskinesis. If loculation of the fluid occurs in the loose connective tissue then a cyst can form. A cyst may also form if urine washes out the epithelium of cell nests of von Brunn. In either case the result is a potential source of weakness as now the epithelium of the calyx and the venous sinuses become the outer limits of parts of the cysts. Any changes of the fornix whether they be the effects of pressure, stasis, infection, or hypoxia, are likely to lead to rupture of the unsupported walls of the venous sinuses and epithelium of the calyx with the formation of veno-calyceal canals. The finding of fornical hæmorrhages or iron pigment deposition in 20 per cent of the unselected cases studied show that hæmorrhages occur frequently in this area. Fortunately, however, it is only occasionally that a persistent open venous canal occurs.

Overgaard (1966) has demonstrated radiologically that the same lesion may persist for months. Clearly, normal repair processes are ineffective. As coagulation is the principal mechanism for sealing vascular leaks it is possible that solid clot formation does not occur because of the fibrinolytic activity of both the urine due to urokinase and of renal venous blood. Renal venous blood in particular has been shown to have considerably greater fibrinolytic activity than renal arterial and systemic venous blood (Poller, 1969). The renal fornix is in fact a site of bleeding where clotting is less likely to occur than elsewhere and if epithelialisation of the fistulous canal takes place, healing may never occur.

Further comment is warranted in regard to the overall topography of the lesions in cases 2 and 3 for they were virtually identical and are depicted diagrammatically (Fig. 7). Of note was the telangiectasia of the vessels of the papilla below the lesion which demonstrates that local lesions of the papilla and fornix can be associated with telangiectasia of papillary vasculature. Only very detailed pathological examination is likely to demonstrate their relationship. Some of the reports in the literature pertaining to hæmorrhagic papillitis, papillary varicosities and angiomas may well be secondary to localised renal fornical lesions.

Clinical diagnosis of renal fornical hæmorrhage is possible in many instances. Pytel (1970) demonstrated the communicating channel in 12 patients by intravenous pyelogram or more often by retrograde pyelography. In the latter procedure hydrogen peroxide was sometimes added to the contrast medium (Klami, 1954). Recently Cihak *et al.* (1969) demonstrated a bleeding site by a careful angiographic technique in which the initial test-dose injection of contrast was not given and a rapid sequence of early films were taken. If the careful and thorough techniques outlined above had been used in our patients we might well have delineated the exact site of bleeding.

It is important to make the diagnosis of renal fornical hæmorrhage for it is only then that conservative therapy can be instituted without the fear that the hæmaturia is due to a small neoplasm. Although surgery has been performed in most reported series, Pytel (1970) successfully used conservative treatment in some cases. Finkle *et al.* (1954) reported 19 cases of which 10 cleared spontaneously with bed rest alone and only 5 eventually required nephrectomy. These authors stressed that those patients treated conservatively must be followed up closely because of the possibility of small neoplastic lesions also responding to conservative measures and they suggested intravenous pyelography at 3-monthly intervals.

Many conservative régimes have been used and variable success has been claimed for each method. Bed rest with transfusion are common to all supplemented by treatments with vitamins C or K, various coagulants, bee, cobra and moccasin venom, methylene blue, steroids and œstrogens. Lavage of the renal pelvis with retrograde media, silver nitrate, methylene blue, ephedrine and adrenaline has been used with benefit.

Radiation to the affected kidney was used to good effect by Mathes and Mayer (1961) hæmaturia ceasing after 1,500 rads in 6 of 8 cases and becoming microscopic in the other 2. One of these subsequently relapsed and required surgery. Despite this success radiotherapy should be used cautiously. A dose as little as 400 rads has been shown to temporarily impair renal function (Avioli *et al.*, 1963) and in view of the often insidious nature and long latent period of radiation nephritis and hypertension (Luxton, 1961) careful follow-up of patients treated by this method is essential to assess long-term complications.

Epsilon-amino-caproic acid (EACA) should be considered in the management of these cases. EACA is an anti-fibrinolytic drug which blocks the plasminogen activator by competitive inhibition (Alkjaersig *et al.*, 1959). Its structural similarity to lysine and arginine enables it to compete with plasminogen as an enzymatic substrate for activator substance (Bergin, 1966). Although many complications have been reported (Bergin; Ratnoff, 1969) it has been used for urological bleeding with few serious side-effects (McNichol *et al.*, 1961; Nilsson *et al.*, 1966; Kirkman, 1967). In the urine it acts by inhibiting urokinase and because 80 per cent of EACA is excreted unchanged in the urine, smaller doses can be used to obtain adequate urinary levels and so further decrease the risk of complications (Haygood *et al.*, 1971). If, as has been postulated, persistent renal fornical hæmorrhage is related to urokinase and fibrinolytic activity of renal venous blood, then EACA is a logical form of therapy and should be given in the dose of 8 g. per day.

Surgery is necessary if bleeding is severe, repeated transfusions are required, or when a neoplasm cannot be excluded. Conservative surgery should be considered in all cases and is possible provided a diagnosis of veno-calyceal fistula can be made pre-operatively or can be confirmed at operation by the pathologist's examination of the fresh specimen. Nephropexy and decapsulation have been used successfully in a few cases but we believe partial nephrectomy is the better operation when a veno-calyceal canal has been demonstrated as the bleeding site is removed. Total nephrectomy will still be necessary for severe bleeding whose exact source cannot be identified, or when malignancy cannot be excluded.

Mr E. England and Mr S. Watson cared for these patients and kindly gave us permission to publish the clinical details. Dr J. Blackwell provided the pathological material in case 2. The illustrations were prepared by the Departments of Medical Illustrations, University of Western Australia, and Royal Perth Hospital.

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RENO-COLIC FISTULA DEMONSTRATED BY ANTEGRADE PYELOGRAPHY

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A FISTULOUS communication between the kidney and the colon is rare and usually causes severe damage to the kidney necessitating nephrectomy. It is the commonest of the reno-alimentary fistulæ, and 110 cases had been reported up to 1958 (Downs, 1958). Reno-duodenal fistulæ are the next most common type (McEwan, 1968), whilst reno-gastric and reno-enteric fistulæ are rarer. Reno-colic fistula was caused by tuberculosis in 28 per cent, by calculous pyonephrosis in 26 per cent, and by non-calculous pyonephrosis in 13 per cent of the 89 cases collected from the literature by Abeshouse (1949), and had also followed perinephric abscesses, and rupture of hydronephroses and hydatid cysts. Trauma to the kidney, both with and without penetrating injury, has resulted in a fistula (Brown, 1966) and the unusual cutaneo-reno-colic fistula may follow the incision of a perinephric abscess (Gibelli, 1968) or blunt trauma to a tuberculous kidney (Eganov and Urusov, 1969). Two reno-colic fistulæ have been found in association with a carcinoma of the kidney (Thompson and Douglas, 1954; Fetter and Varano, 1956) and necrosis following irradiation for a carcinoma of the bladder was thought to be responsible in another patient (Gibbons and Schmidt, 1965). In contrast to lower urinary tract fistulæ, in which the primary cause is usually in the bowel, no reno-colic fistula has been reported as the result of disease in the colon.

It has been suggested that the condition has become less common because of improved methods of diagnosis and treatment of renal disease (Arthur and Morris, 1966), but this view has been challenged by Shukri (1968), and Hobson and Munyan (1960) consider that reno-colic fistulæ are found more frequently because of improved radiological methods of diagnosis. In the majority of cases the affected kidney is non-functioning on excretion urography, although one fistula was shown by this method (Schmidt, 1968) and a fistula from a sole surviving kidney was successfully treated by Rost *et al.* (1956).

Percutaneous antegrade pyelography is useful in the investigation of non-functioning kidneys (Lundin and Wadström, 1956) and may allow cystoscopy to be avoided (Budd, 1970). The procedure takes place in the X-ray department. The patient lies prone and after infiltration of the skin with local anæsthetic, a fine exploring needle is introduced into the kidney under X-ray control, using image intensification and a television monitor. A case is described here in which the method has been used to demonstrate a reno-colic fistula.

Case Report.—A 42-year-old West Indian housewife, who had lived in England for 11 years, was seen at the Bristol Royal Infirmary with a 3-month history of pain in the right loin associated with the passage of intermittently dark urine. Culture of the urine before admission produced a growth of *E. Coli*, but no acid-fast bacilli were seen and the patient was treated with Septrin. The patient had had one episode of diarrhœa and vomiting 2 months before she was seen, but had no other change in bowel habit, and had no history of previous urinary tract infection. Since the illness started she had lost a considerable amount of weight. On examination, the patient was anæmic and had a palpable hard smooth right kidney, but no other relevant abnormality.

Investigations.—Iron deficient anæmia with Hb. 7·7 Gm./100 ml. W.B.C. normal, E.S.R. 60 mm./hr. Serum urea and electrolytes normal. Subsequent urine cultures were sterile, although on microscopy pus cells were still present. Guinea-pig inoculation for acid-fast bacilli was done. A chest X-ray was normal.

Excretion Urography.—A normal left kidney was demonstrated. On the right side gas was present in the renal pelvis in the supine position and no renal excretion was seen (Fig. 1, A). A calyceal pattern was shown with the patient in the prone position (Fig. 1, B), and a fluid level was present in the renal pelvis in an erect film (Fig. 1, C).

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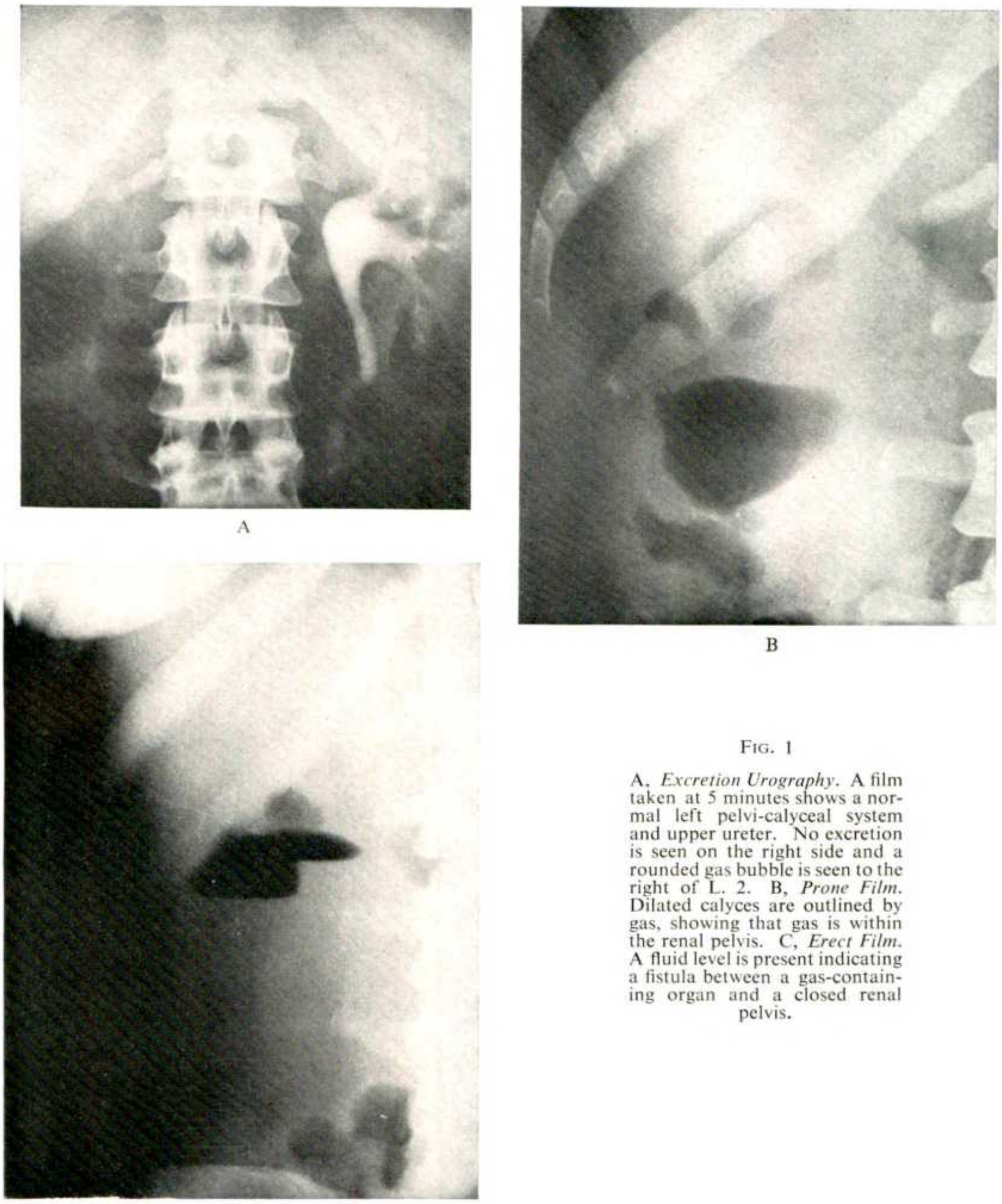


A

B

C

FIG. 1

A, *Excretion Urography*. A film taken at 5 minutes shows a normal left pelvi-calyceal system and upper ureter. No excretion is seen on the right side and a rounded gas bubble is seen to the right of L. 2. B, *Prone Film*. Dilated calyces are outlined by gas, showing that gas is within the renal pelvis. C, *Erect Film*. A fluid level is present indicating a fistula between a gas-containing organ and a closed renal pelvis.

Cystoscopy.—Pus was seen coming from the right ureteric orifice, and there were inflammatory changes in the surrounding bladder wall. Catheterisation of the right ureteric orifice was impossible beyond 3 cm., and retrograde injection of contrast medium was unsuccessful.

Antegrade Pyelography.—Was performed percutaneously. Fæcal-smelling brown pus was aspirated, and 40 ml. of Hypaque 25 per cent were injected. This outlined a hydronephrotic kidney and delayed films showed a track from the lower calyx to the colon. (Fig. 2).

FIG. 2

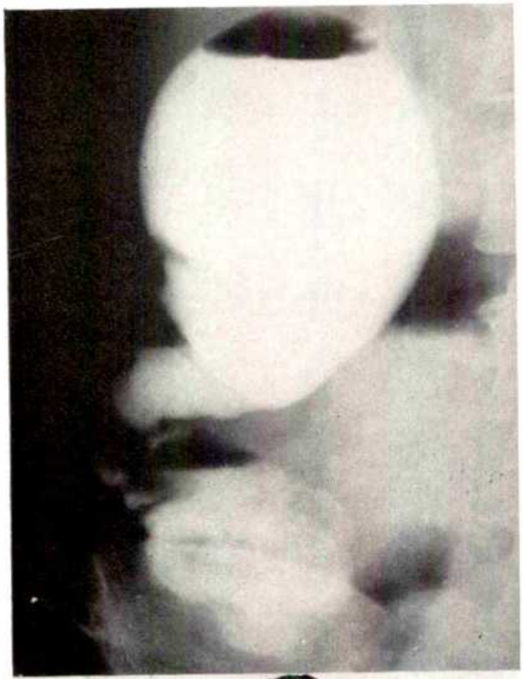
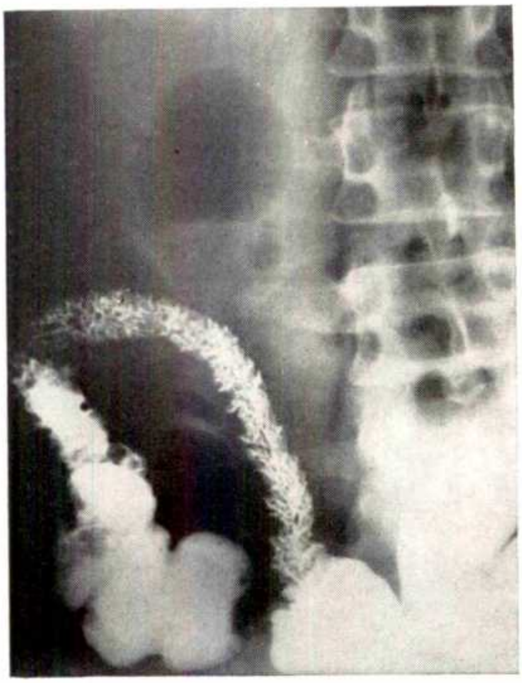


FIG. 3



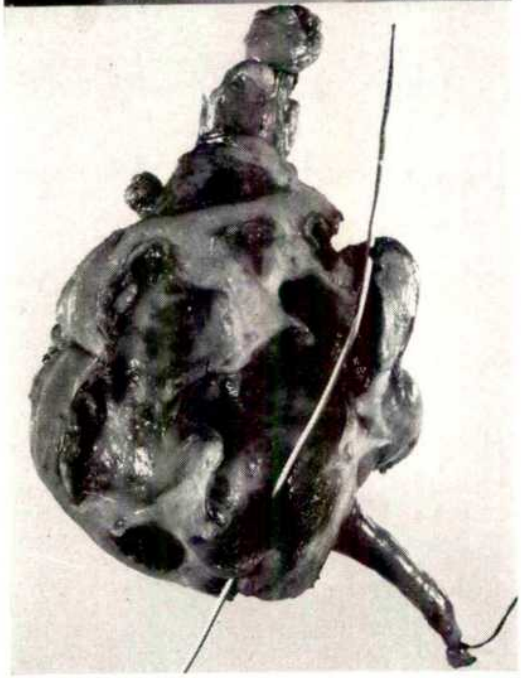


FIG. 4

Fig. 2.—*Antegrade Pyelography, Erect Film.* Contrast medium is seen in the renal pelvis and a fluid level is present. A track leads laterally from the lower end of the pelvis to the ascending colon, which contains gas and contrast medium. No ureteric drainage occurred.

Fig. 3.—*Barium Enema.* The hepatic flexure shows a normal mucosal pattern with no barium outside the lumen of the colon. Gas is again present in the kidney.

Fig. 4.—*Excised Kidney after Bisection.* A probe demonstrates the site of the fistula which extended from the lower calyx to the ascending colon.

Barium Enema (Fig. 3).—Showed no communication between the colon and the kidney and a normal mucosal pattern was present.

Treatment and Progress.—The patient developed a swinging pyrexia and the mass in the right loin gradually increased in size. It was thought likely that the lesion was due to a tuberculous infection and since guinea-pig inoculation had already been done and the patient's condition was deteriorating, it was considered justifiable to give Streptomycin, PAS, and INAH in preparation for surgical intervention. Three weeks after admission the right kidney was explored through a 12th rib loin incision. It was found to be acutely inflamed and adherent to perinephric fat, with a short fistula between the lower calyx and the ascending colon (Fig. 4). A nephrectomy was performed, and the colonic defect closed in two layers. Apart from a wound infection the post-operative progress was satisfactory and the patient was discharged home 4 weeks after operation. Histological examination of the excised kidney showed pyelonephritis with no evidence of tuberculosis.

DISCUSSION

Before the advent of modern radiological methods the diagnosis of reno-colic fistula was usually made at post-mortem (Abeshouse, 1949). The diagnosis may still be made in this way (Gibbons and Schmidt, 1965), or an unsuspected fistula may be found at operation (Derevyanko, 1965; Petri, 1960). Difficulty in making the diagnosis arises from the variable symptoms with which the patient may present. Most patients have symptoms of long-standing renal infection, and the patient reported here is unusual in having only a 3-month history. Loss of weight and the onset of diarrhœa in a patient with long-standing renal infection may suggest the diagnosis (Popluca and Badea, 1963). In one case a renal stone was passed per rectum (Narins and Segal, 1959) and in another a staghorn calculus caused an intestinal obstruction (Downs, 1958). Cutaneo-reno-colic fistulæ usually present with fæcal drainage from a wound (Rodrigues-Netto *et al.*, 1967).

TABLE

Radiological Methods of Diagnosis Described in 43 Cases Reported Since 1949

Investigation	Total	Diagnostic of Fistula
Plain abdominal X-ray	29	4
Excretion urography	34	1
Retrograde pyelogram	34	23
Barium enema	21	9
Sinogram	8	6
Aortogram	1	0
Antegrade pyelogram (present report)	1	1

The existence of a fistula from a functioning kidney can be proved by the passage in the fæces of indigo carmine injected intravenously or methylene blue given by mouth (Ellik and Getz, 1953), but this does not demonstrate the site of the fistula. Gas in the kidney may be difficult to recognise in a single film because of overlying bowel gas, but if present indicates either a fistula, infection, or recent surgical intervention (Kent, 1955). Excretion urography is valuable in demonstrating the condition of the opposite kidney, but the affected side usually does not function. Retrograde pyelography is the investigation that has proved most successful, but the ureter may not be easy to catheterise or the fistula may not be shown. The method has failed in 11 cases out of 34 where it has been used (Table). The fistula may sometimes be shown by a barium enema (Bocchi and Traversin, 1965; Schönebeck and Hjortsjö, 1966) and delayed films may show barium in the kidney. Aortography was of no diagnostic help in the one case in which it has been reported (Ellik and Getz, 1953). In those cases with a cutaneous fistula, sinography is the obvious investigation, but even this may not always show the communication (Thompson and Douglas, 1954). The results of the radiological investigations performed in 43 cases recorded since 1949, including the present case, are summarised in the Table. Twenty-seven of these cases have been reported since the review by Downs (1958).

Percutaneous antegrade pyelography was introduced by Wickbom (1954) and has proved a safe, simple and accurate method of investigation (Jeans *et al.*, 1972). It allows the contents of the renal pelvis to be cultured without contamination, and enables an immediate distinction to be made between a hydro- and a pyonephrosis. The cause of the obstruction and any complications which may have occurred can usually be demonstrated.

SUMMARY

A case is reported in which a reno-intestinal fistula was suspected when air was seen in a non-functioning kidney, and the diagnosis of reno-colic fistula was made by percutaneous antegrade pyelography. The methods used to establish the diagnosis in 43 cases recorded since 1949 have been reviewed. Since none of the methods of investigation has always been reliable it is suggested that antegrade pyelography may be a valuable diagnostic procedure in this rare condition.

We are grateful to Mr J. P. Mitchell for permission to report this case which was admitted under his care, and to Mr Mitchell, Dr J. Roylance and Mr J. C. Gingell for their advice. The photographs were kindly produced by Mr J. Eatough of the Department of Medical Illustration of the United Bristol Hospitals.

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THE URETEROVESICAL INNERVATION

A New Concept Based on a Histochemical Study

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THE classical concept of the innervation of the urinary tract pretends that the ureter is supplied by sympathetic nerves while the bladder receives essentially parasympathetic nerves.

Morphological studies of the intrinsic innervation of the urinary tract have been limited for decades by classical microscopic techniques (such as intravital methylene blue or silver impregnation) which could not establish the difference between sympathetic (adrenergic) and parasympathetic (cholinergic) nerves.

The application of new and highly specific histochemical methods for the demonstration of adrenergic (norepinephrine) and cholinergic (acetylcholinesterase) nerve elements has thrown new light on the organisation and dynamics of the autonomic innervation of the mammalian ureter and bladder.

Material and Methods.—Specimens were taken from the ureters and bladders of 25 mongrel dogs and 5 rabbits. The tissues studied were excised under light intravenous nembutal anæsthesia and specimens were obtained from all levels of the ureter and bladder. The tissues were quickly frozen in liquid nitrogen and sectioned in a cryostat at −30°C. Transverse and sagittal serial sections of 10 to 20 μ were selected every 100 to 200 μ. At the level of the ureterovesical junction, serial sections were taken each 40 μ. The sections were mounted on a frosted slide and subsequently stained after the different histochemical methods.

Cholinergic nerve elements were studied by the technique of Karnovsky and Roots (1964) as modified by El-Badawi and Schenk (1967) for the demonstration of acetylcholinesterase (AChE).

AChE activity is characterised by a fine granular reddish-brown precipitate. The sections were studied under a Zeiss photomicroscope by ordinary light, phase contrast microscopy and Nomarski differential phase microscopy.

Adrenergic nerves were demonstrated by the formaldehyde-induced fluorescence of catecholamines following the method of Falck *et al.* (1962) as modified by Spriggs *et al.* (1966). The sections were examined under a Zeiss fluorescent photomicroscope using a high-pressure mercury lamp, a BG 12 excitation filter and a 470 μ barrier filter. Under these conditions the specific fluorescence of norepinephrine (NE) is identified by a yellowish-green fluorescence localised in varicosities along the sympathetic nerve fibres and in granular formations in the cytoplasm of adrenergic neurons (for details see Corrodi *et al.*, 1967).

The distribution of *monoamine oxidase* (MAO) activity was studied histochemically by the method of Glenner *et al.* (1957). The sites of MAO activity are identified by deposits of a bluish-purple formazan pigment developed when tryptamine is oxidised by MAO following the reduction of nitroblue tetrazolium.

RESULTS

This paper is limited to the description of the essential features of the ureteral and vesical innervation as they appear under this new approach.

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The ureter and bladder of mammalian animals (dog-rabbit) is characterised by a *dual* sympathetic (adrenergic) and parasympathetic (cholinergic) innervation (Figs. 1, 2 and 3). This is confirmed by the studies of Duarte-Escalante *et al.* (1969) and Elbadawi and Schenck (1966-1969). The nerves enter the organ following the course of the blood vessels. They ramify into the different layers of the ureter and bladder. In both organs the nervous pattern is characterised by perivascular plexuses supplying the muscular and subepithelial layers as well as the accompanying vessels (Fig. 4).

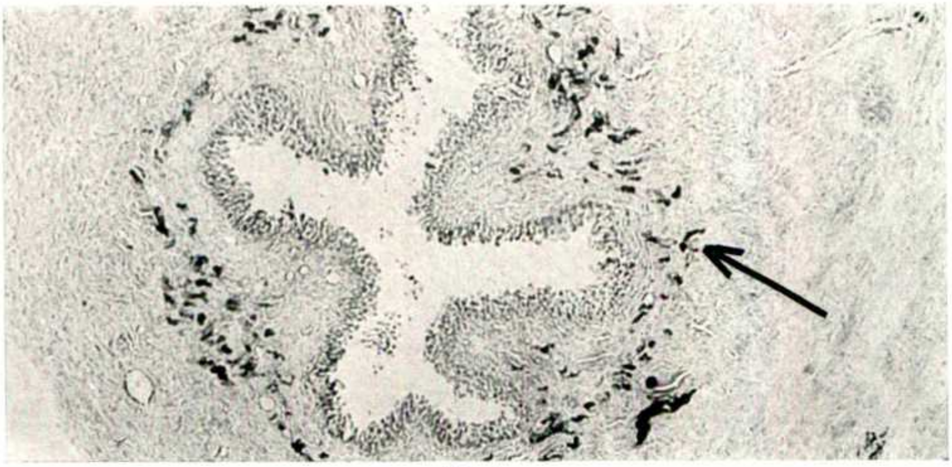

FIG. 1

Upper ureter—acetylcholinesterase (AChE). × 50. Only a few cholinergic nerves (arrow) are observed scattered in the subepithelial layer.

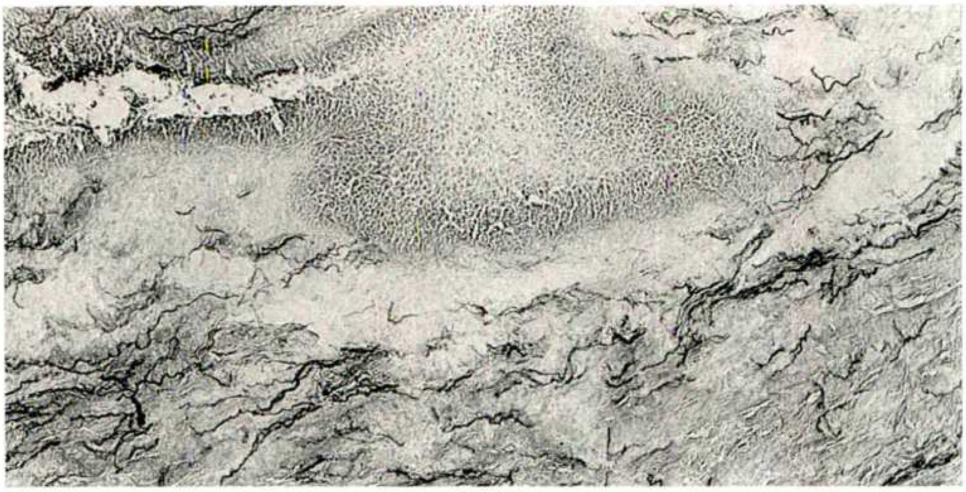

FIG. 2

Terminal ureter—oblique section—AChE. × 80. Extensive ramifications of the cholinergic nerve fibres in the muscular and subepithelial layers.

In the ureteral musculature, the nerve fibres are related to small bundles of muscle so that the nerve-muscle ratio is low (1/50) for both sympathetic and parasympathetic components. In the bladder, the nervous plexus is related to individual muscle cells by a 1/1 nerve-muscle ratio for the parasympathetic components, and a somewhat lower ratio for the sympathetic elements (Fig. 5). In the dome of the bladder, the sympathetic nerves are less abundant than in the base of the organ.

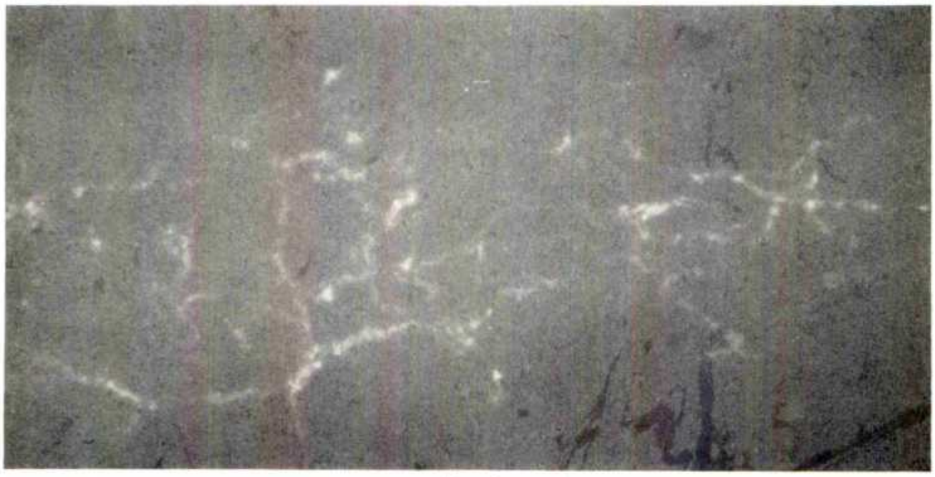

FIG. 3

Mid ureter—fluorescent catecholamines. × 125. Typical adrenergic nerve terminals in the muscular layer.

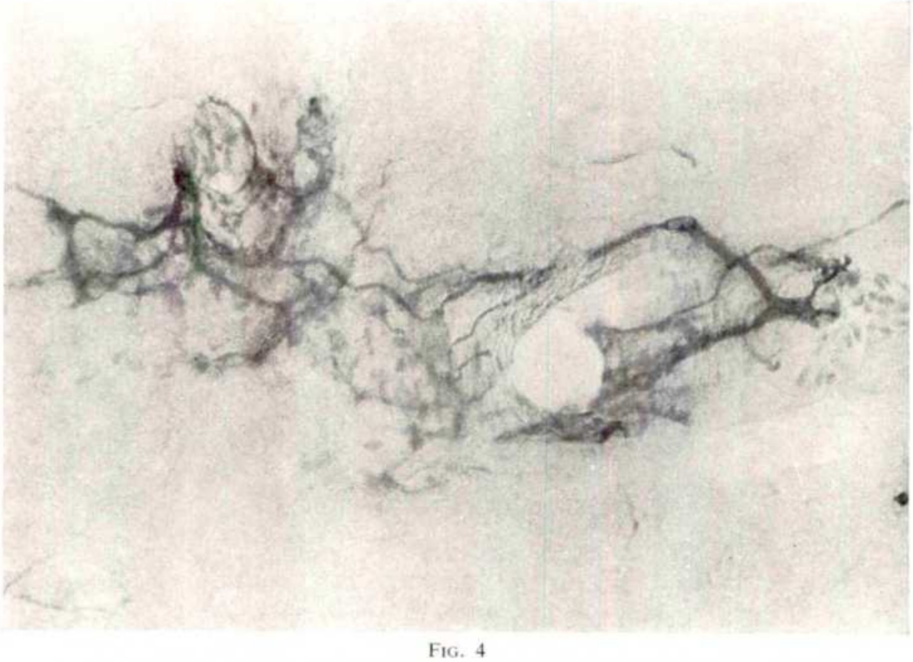

FIG. 4

Terminal ureter—AChE. × 1250. Perivascular plexus around subepithelial arterioles.

In the ureter, there is a progressive distalward increase in the density of the nervous network. The terminal ureter is richly innervated, while at the level of the pyeloureteral junction only a few nerve fibres are observed.

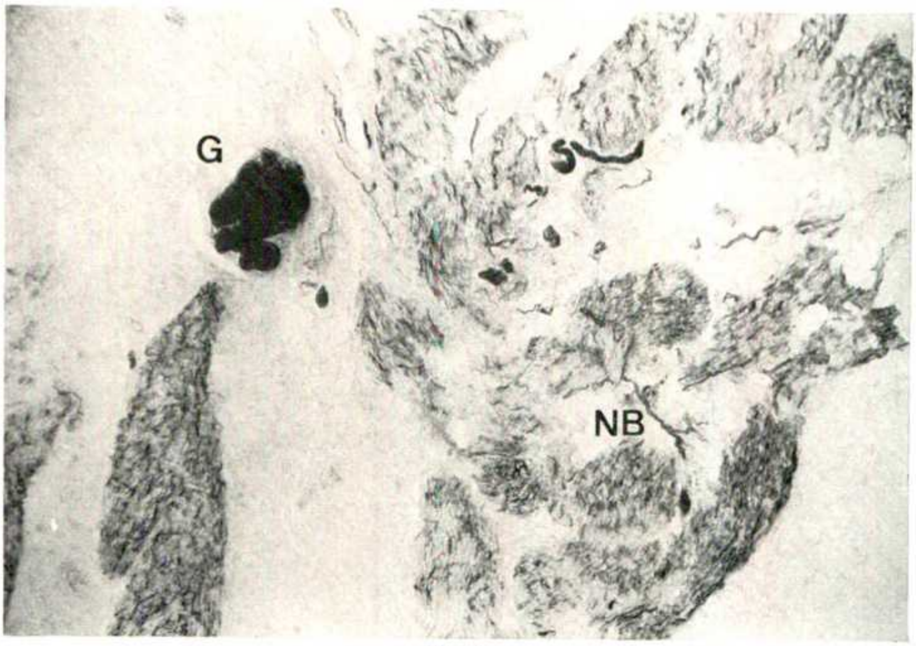

FIG. 5

Bladder base—dog—AchE. × 60. Large cholinergic nerve bundle (NB) with its terminal muscular ramifications. A cholinergic ganglion (G) is observed between muscle bundles.

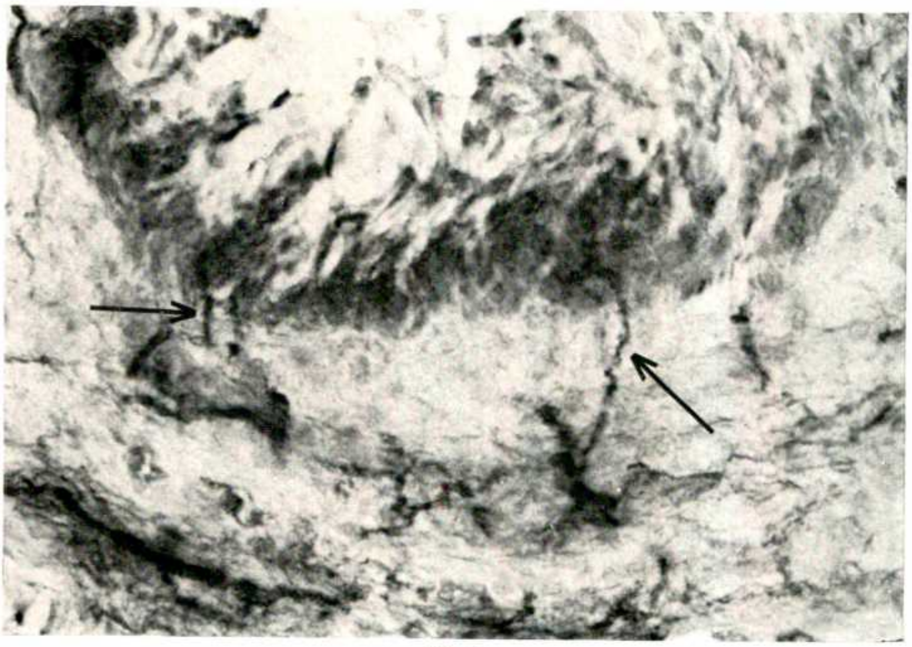

FIG. 6

Terminal ureter—Ach.E. × 500. Cholinergic subepithelial nerve bundles give rise to epithelial terminal fibres.

Species differences exist, for instance in the rabbit's ureter nerve fibres penetrate the basement membrane of the epithelium while in the dog the epithelial layer is not innervated (Fig. 6). Adrenergic nerves are rare in the dog ureter compared to the rabbit.

At the level of the ureterovesical junction a fibromuscular sheath surrounds the last centimetres of the ureter and forms a peri-ureteral sleeve which is commonly designated as Waldeyer's sheath. The innervation pattern of this important anatomical structure is identical with the nervous network of the vesical musculature and definitely different from the innervation of the ureteral musculature (Fig. 7). This suggests that Waldeyer's sheath is a structure of endodermic origin and belongs to the bladder musculature in contradiction to the theories advanced by Tanagho and Pugh (1963).

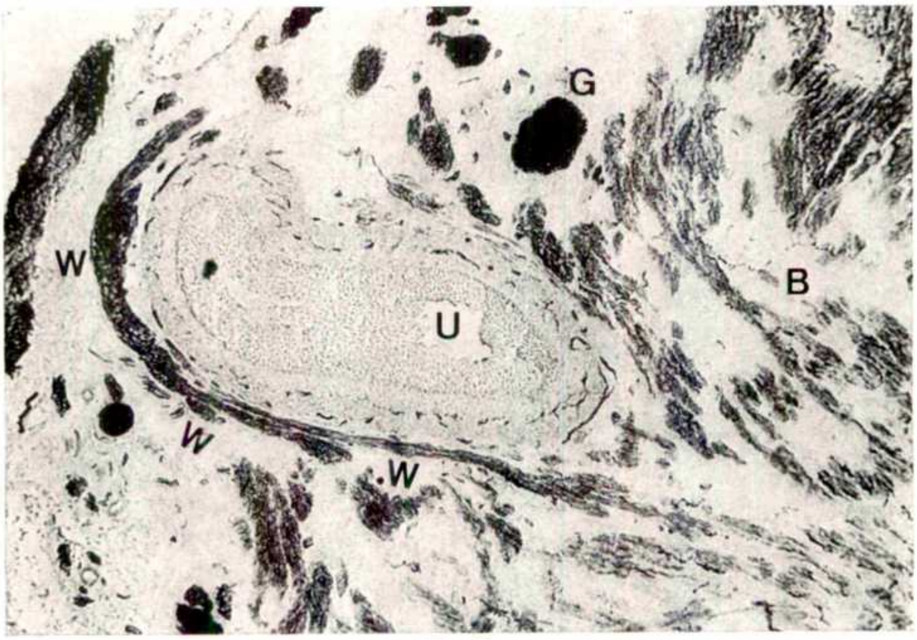

FIG. 7

Ureterovesical junction—AchE. × 60. Important difference between the density of the detrusor innervation (B) and the one of the ureteral musculature (U). Innervation of Waldeyer's peri-ureteral muscular sheath (W) is identical with the bladder musculature. Numerous ganglia (G) are observed at the level of the ureterovesical junction.

In the bladder, ganglia are most commonly found in the base and around the ureteral orifices. They are part of a ureterovesical ganglionic complex which includes a large number of ganglion cells located:

1. in the adventitia and the connective tissue enclosing the terminal ureter and bladder base;
2. in the musculature of the bladder base surrounding the trigone;
3. between the intramural ureter and the surrounding vesical musculature;
4. contiguous to the peri-ureteral musculature (Waldeyer's sheath);
5. between the peri-ureteral musculature and the ureter (Fig. 8).

Ganglia are extremely sparse or absent in the middle and upper ureter.

The ureterovesical ganglia are part of the pelvic plexus which receives branches from the pelvic and hypogastric nerves (Kuntz and Moseley, 1936; Bradley and Teague, 1968). They are composed by a majority of cholinergic cells since their cytoplasm is filled with AChE granules; a few cells, however, do not exhibit any AChE activity (Figs. 9 and 10).

Those ganglia are thus mainly parasympathetic (cholinergic) but must be considered as mixed structures since it is possible to demonstrate the existence of adrenergic nerve elements in those structures (Fig. 11). Using the localisation of fluorescent catecholamines, adrenergic elements are characterised by ganglion cell bodies showing different degrees of fluorescence, varying from quite faint to very high intensities. The fluorescent cells are rather uniform in size, arranged in clusters or scattered in these ganglia. Among the fluorescent nerve cells, groups of completely non-fluorescent cells are noted. Fluorescent axonial process is observed extending from fluorescent cells. In addition to the fluorescent cells, adrenergic nerve terminals are seen between and around ganglion cells. These intensely fluorescent adrenergic nerves often terminate in close contact with ganglion cells, which sometimes are completely surrounded by a basket of fluorescent fibres showing abundant varicosities which are considered as the morphological sites of synapses (Hamberger *et al.*, 1965) (Fig. 12).

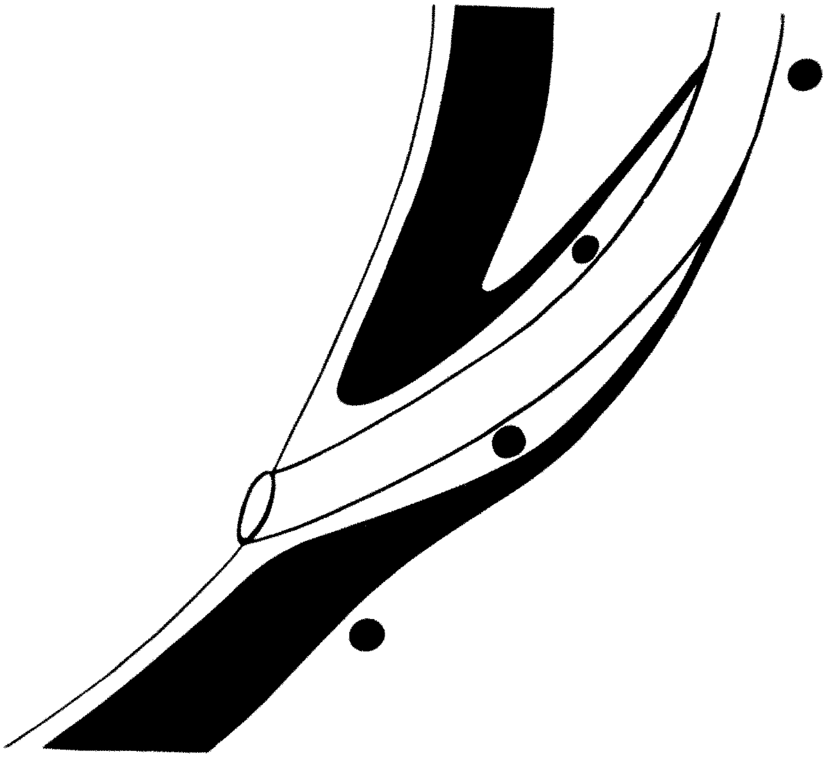

FIG. 8
Schematic representation of the mixed cholinergic-adrenergic ureterovesical ganglionic complex.

The demonstration of sympathetic nerve terminals in parasympathetic ganglia raises the possibility of new mechanisms for adrenergic influence on ganglionic activity and will be further discussed in this paper.

The ureterovesical ganglionic complex is not only composed of intraganglionic neurons, but includes also extraganglionic cells represented by intramural nerve cells in the lower ureter and bladder. Controversy has been raging for decades about the existence of intramural ganglion cells in the ureter. In this study, according to morphological and histochemical criteria, a ganglion cell is characterised by storage of either acetylcholinesterase or norepinephrine in the cytoplasm and the existence of an axon on serial sections. Intramural nerve cells, either adrenergic

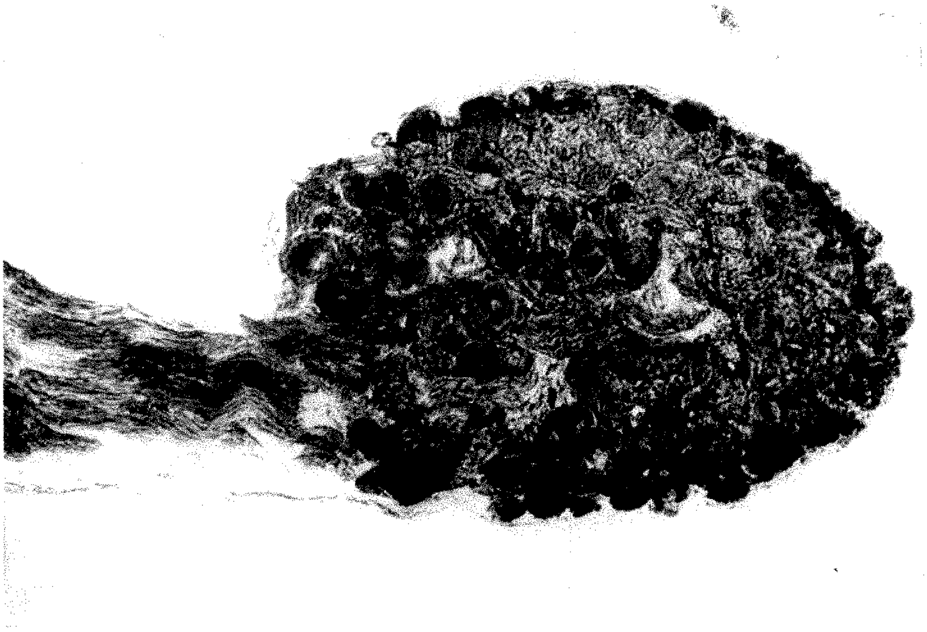

FIG. 9

Ureterovesical ganglion—AchE. × 125. Characteristic aspect of a ureterovesical ganglion composed by a majority of cholinergic ganglion cells. The ganglion is joined by its related nerve trunk.

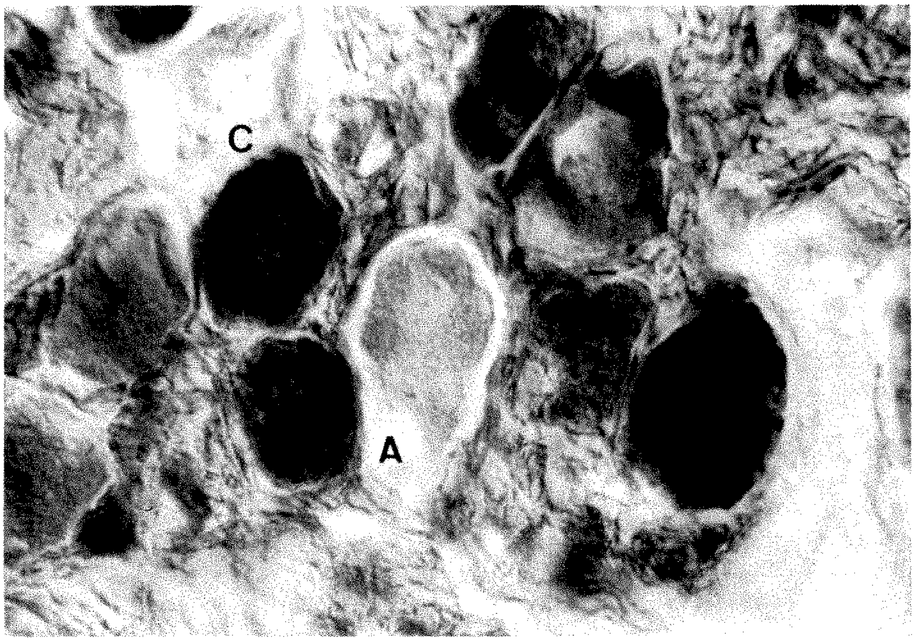

FIG. 10

Ureterovesical ganglion—AchE. Nomarski interferential phase microscopy × 500. Most cells show a cytoplasm filled with AchE granules (C) but some cells do not exhibit any AChE activity and appear very pale (A); they represent adrenergic ganglion cell in a mixed cholinergic-adrenergic ganglion.

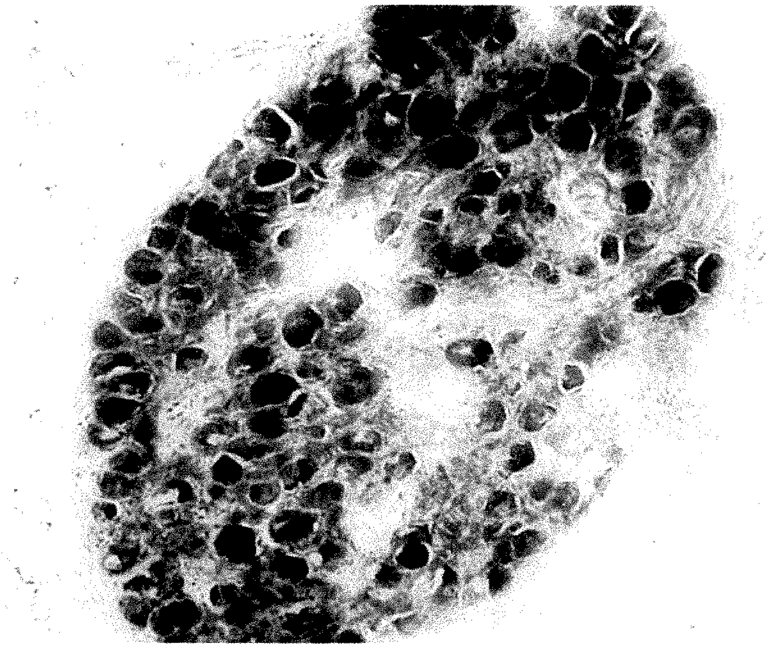

FIG. 11

Ureterovesical ganglion—monoamine oxidase (MAO). ×125. The cytoplasm of the ganglion cells exhibits a moderate or strong MAO activity.

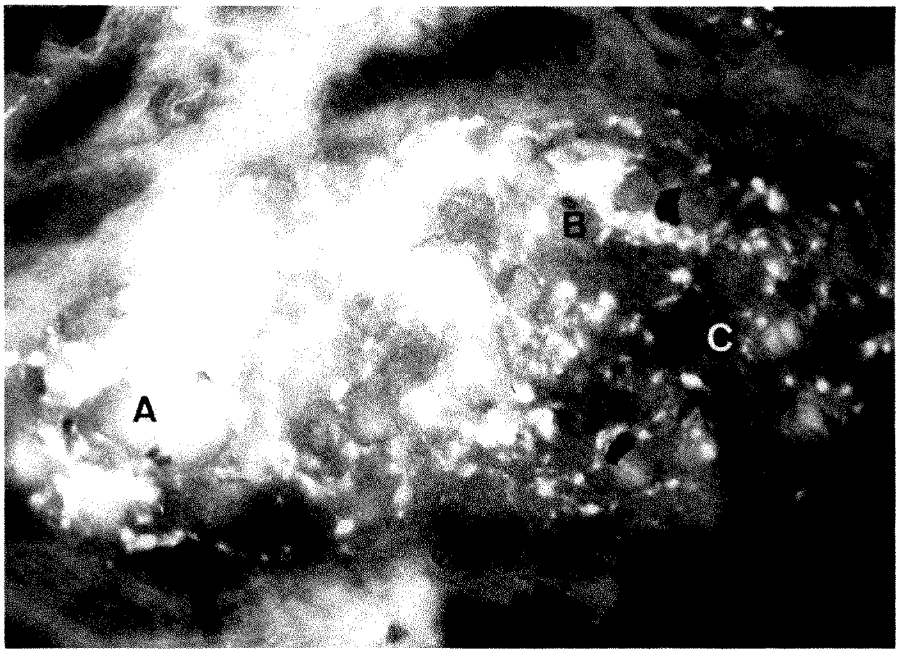

FIG. 12

Ureterovesical ganglion—fluorescent catecholamines (NE). ×125. Mixed ureterovesical ganglion composed of highly fluorescent (A) (adrenergic) and non-fluorescent (C) (cholinergic) ganglion cells. Fluorescent adrenergic nerve terminals surround numerous ganglion cells (B) and are considered to be synaptic structure.

or cholinergic, are usually associated with blood vessels (Fig. 13). Isolated cells are also present in the muscular and subepithelial layer (Figs. 14 and 15). This system is especially well developed at the ureterovesical junction.

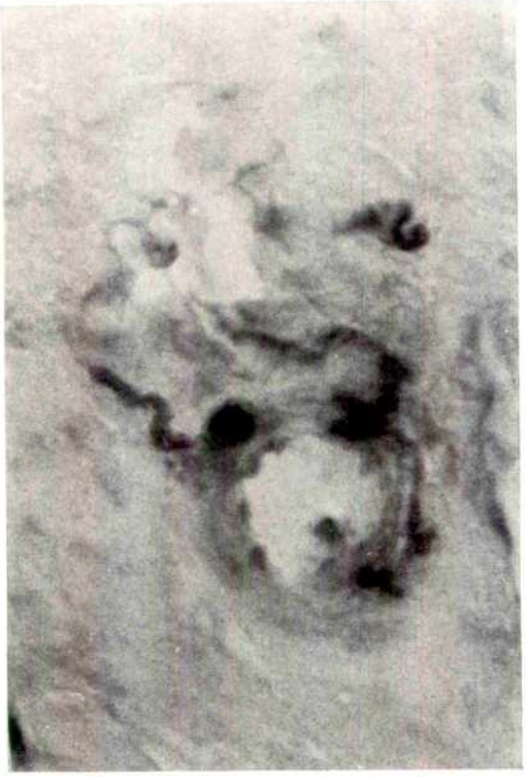

FIG. 13
Intramural ureter—AchE. × 1000. Two cholinergic nerve cells are observed adjacent to a small arteriole. Intramural ganglion cells are usually associated with blood vessels.

DISCUSSION

The classical concept of the autonomic nervous system maintains that peripheral sympathetic ganglion cells are located in the sympathetic chain or the prevertebral ganglia while the peripheral parasympathetic ganglion cells are found in close vicinity to the innervated organs (Fig. 16). It was previously generally believed that no interaction occurred between neurons in autonomic ganglia or between the sympathetic and parasympathetic system (Kuntz, 1953). According to this classical view, all preganglionic fibres are cholinergic in the sympathetic ganglia and no adrenergic elements are believed to exist in these ganglia.

It has been suggested, however, from physiological and pharmacological experiments that catecholamines can modulate sympathetic ganglionic activity (Marrazzi, 1939*a*, *b*; Bülbring, 1944; Pasternak and Larrabee, 1948; Lundberg, 1952; Goffart, 1957; Costa *et al.*, 1961; Trendelenburg, 1961; Curtis, 1963; Giller and Baker, 1963; Reinert, 1963; Weir and McLennan, 1963; Norberg and Sjöqvist, 1966).

There are also some indications for the existence of adrenergic mechanisms in certain parasympathetic ganglia (Tum Suden *et al.*, 1951; McDougal and West, 1954; Kosterlitz and Robinson, 1957; Kewenter, 1965). The fluorescence microscopic technique of Falck and Hillarp

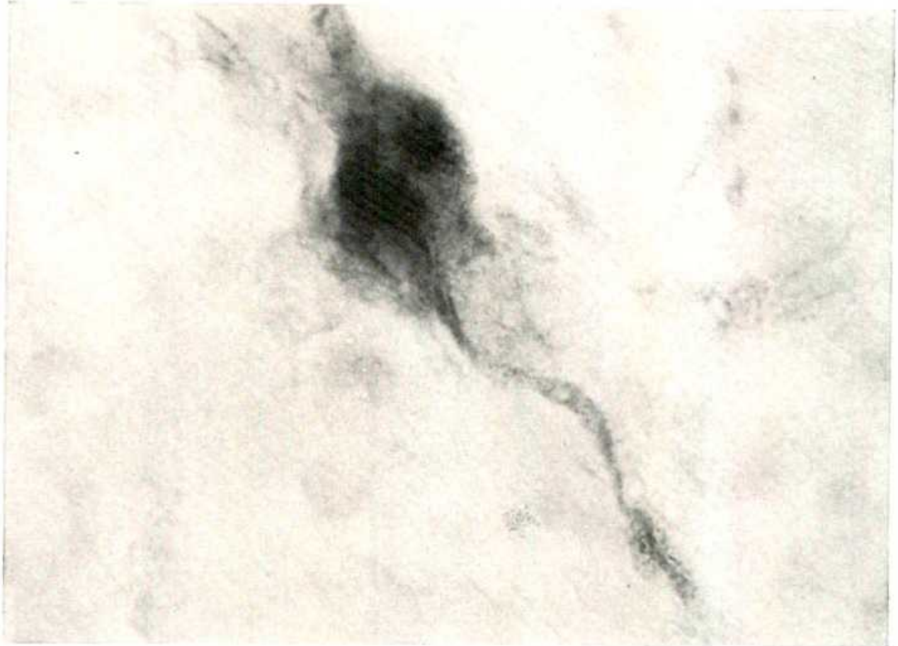

FIG. 14

Terminal ureter—AchE. ×1250. Isolated intramural ganglion cell. The cell has an eccentric nucleus—the cytoplasm exhibits a high AChE activity and the axon is running between the ureteral muscle bundles.

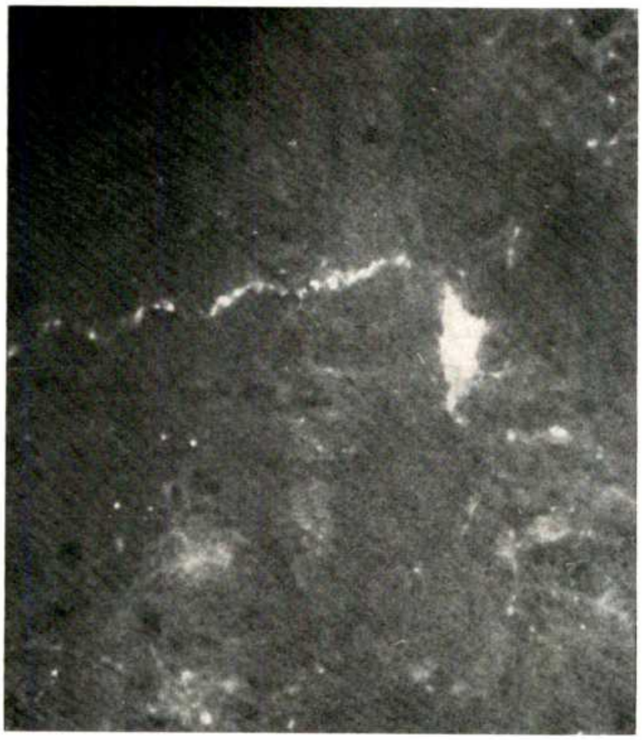

FIG. 15

Terminal ureter—NE. ×600. Fluorescent adrenergic nerve cell and its axon in the muscular layer.

(1962) which directly visualises the adrenergic nerves has provided a morphological correlation to these physiological and pharmacological data. Hamberger *et al.* (1963-1965) demonstrated the existence of adrenergic nerve terminals in sympathetic ganglia, and similar elements were revealed in parasympathetic ganglia of the intestine by Norberg (1964) and in the bladder and male internal genital organs (Hamberger and Norberg, 1965*a*, *b*; El Badawi and Schenck, 1967).

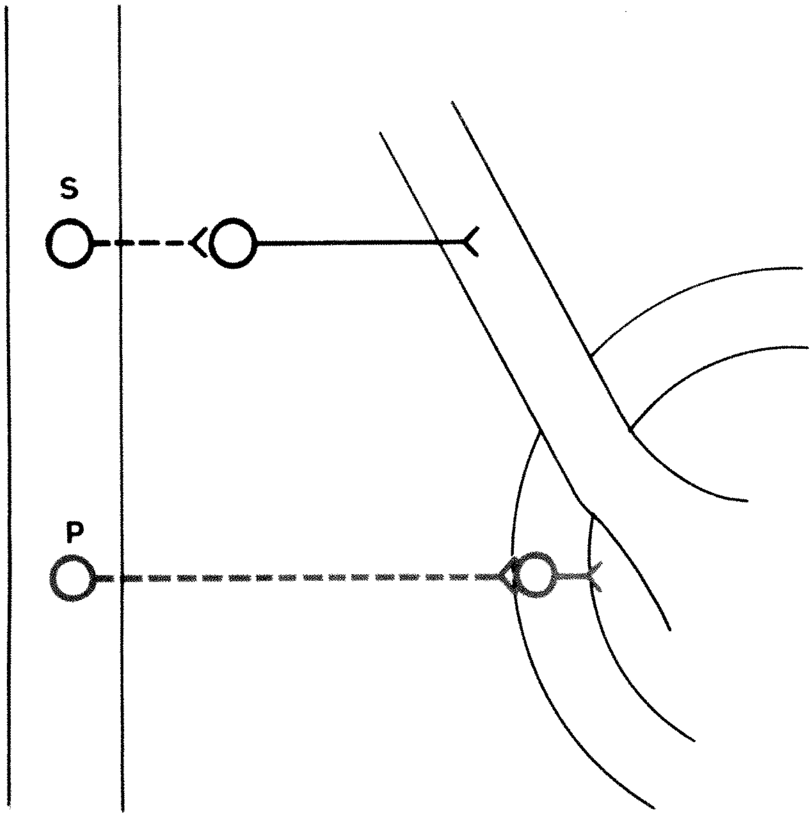

FIG. 16

Classical concept of the peripheral autonomic nervous system. The sympathetic system (S) is characterised by long postganglionic neurons originating from the sympathetic chain or the prevertebral ganglia. The parasympathetic system (P) is composed of short postganglionic neurons located in close vicinity or in the innervated organ.

Our observations give morphological evidence for the existence of adrenergic nerve terminals in parasympathetic pelvic ganglia. The physiological implication of these nerve terminals is emphasised as it seems likely that the adrenergic transmitter norepinephrine may be released in parasympathetic ganglia from the synaptic terminals.

It is thus possible that adrenergic synaptic terminals, which are liable to be found in all sympathetic ganglia (Norberg, 1967) may also be an important feature of the parasympathetic ganglia.

As regards the function of these adrenergic intraganglionic synapses, results of recent experiments indicate a general *inhibitory* action (for review see Norberg and Sjöqvist, 1966).

The other important morphological feature of this autonomic innervation is represented by the existence of sympathetic ganglion cells in the bladder and terminal ureter. These elements are considered to be *short* adrenergic neurons since they derive from postganglionic neurons located close to or within the target organ, in contrast to the classical concept of *long* adrenergic neurons with their cell bodies in the pre- or paravertebral ganglia (Sjöstrand, 1965). The existence of sympathetic ganglion cells in close vicinity to the pelvic organs has been suggested as early as 1895 by Langley and Anderson and recently confirmed by other investigators for different pelvic viscera, principally the vas deferens (Sjöstrand, 1962*a*, *b*; Ferry, 1963; Merrilees *et al.*, 1963; Birmingham and Wilson, 1963; Owman and Sjöstrand, 1965; Sjöstrand, 1965; El-Badawi and Schenck, 1968; Birmingham, 1970).

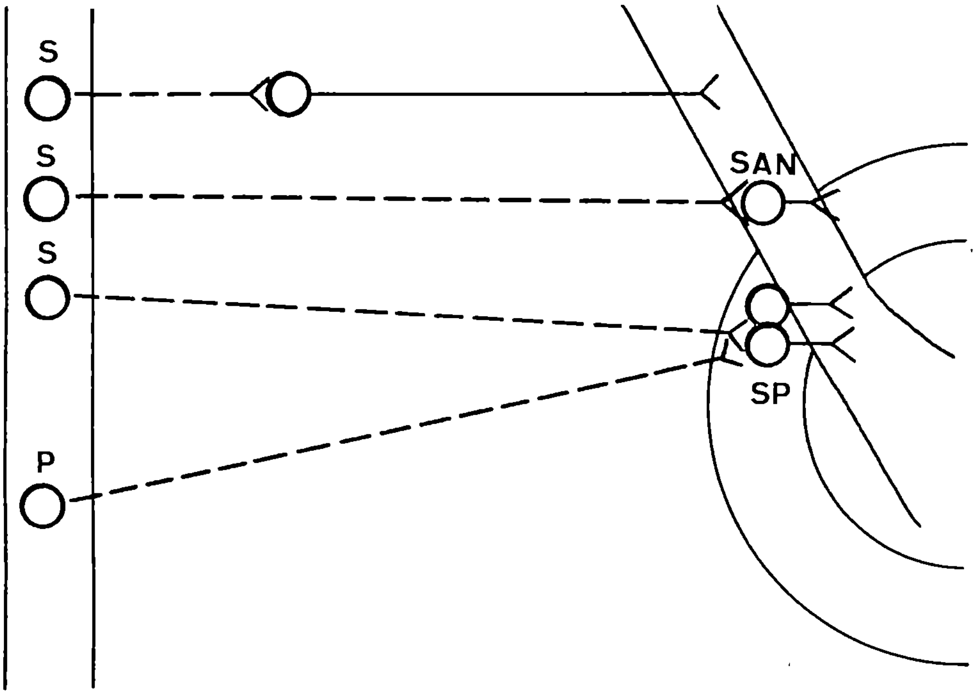

FIG. 17

New concept of the organisation of the peripheral autonomic nervous system. In addition to the classical aspects: (1) Sympathetic neurons are located close to the innervated organ (SAN). This pattern of sympathetic innervation is schematically similar to the parasympathetic system and constitutes a "short adrenergic neuronal system". (2) Post-ganglionic sympathetic neurons terminate in parasympathetic and sympathetic ganglia (SP).

This pattern of sympathetic innervation is schematically similar to the parasympathetic system (Fig. 17). The peculiar pattern of the autonomic innervation implies, for example, that it is impossible to denervate such organs by simple section of their extrinsic nerves since intrinsic ganglion cells are still present. It also explains why conflicting results have been obtained in physiological and pharmacological investigations on the ureter and bladder.

The nerves associated with ureterovesical ganglia innervate the terminal ureter, ureterovesical junction, trigone and bladder base. Hence, those structures are neurologically in continuity with one another and their functions seem to be co-ordinated by both components of the autonomic nervous system.

In the present state of our knowledge, the eventual role played by these nervous structures in the development of congenital malformations of the ureter and bladder remains to be re-evaluated in the light of the present findings.

The existence of a " short " neuronal system is a fundamental feature of the peripheral autonomic innervation. It introduces a new concept of innervation of the urinary tract, since morphological structures suggest the possibility of an interaction of the two components of the autonomic nervous system and of a peripheral mechanism for mutual integration and modulation of the activity of the terminal ureter and bladder.

CONCLUSIONS

The ureter and bladder show a dual cholinergic (parasympathetic) and adrenergic (sympathetic) innervation made of nerve fibres and ganglion cells.

In both organs, the nervous pattern is characterised by perivascular plexuses supplying the muscular and subepithelial layers. Ganglia are essentially found at the level of the ureterovesical junction and constitute a mixed adrenergic-cholinergic ganglionic complex.

Intrinsic sympathetic ganglion cells are located in close vicinity or in the terminal ureter and bladder, they represent " short adrenergic neurons ". Morphological evidence for the existence of sympathetic nerve terminals in parasympathetic pelvic ganglia is presented. These fundamental features of the peripheral autonomic innervation introduce a new concept of the innervation of the urinary tract since morphological evidences are provided for an interaction of the two components of the autonomic nervous system and for the existence of a peripheral mechanism for mutual integration of sympathetic and parasympathetic influences on the activity of the ureter and bladder.

NOTE.—All photomicrographs were taken from the dog except Figures 3, 6 and 7 which are from the rabbit.

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A COMPLICATION OF CRYOPROSTATECTOMY

By John M. O'Brien, M.A., M.B., B.Ch., F.R.C.S., Senior Registrar, and
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DISCUSSION

Although there has been interest in the therapeutic effect of tissue freezing for many years, it was not until 1962 that Cooper pioneered controlled cryotherapy. Considerable interest has subsequently been shown in cryoprostatectomy for the management of prostatic obstruction, and several series have now been reported by Sessia *et al.* (1968), Gill *et al.* (1970) and other workers.

The principal advantages of this procedure are its suitability for those patients, particularly with severe cardio-pulmonary disease, considered too ill to withstand the more conventional forms of treatment, and that it may be performed under local, spinal or light general anæsthesia.

One of the principal difficulties encountered with this technique is the accurate localisation of the cryoprobe within the prostatic urethra, thereby avoiding injuries to structures adjacent to the prostate. Initial attempts at localisation were done by rectal palpation and temperature measurement of the rectal wall, but Sessia (1968), using a modified probe, incorporating thermocouples identified by marker buttons demonstrable radiologically, has considerably reduced this hazard.

Gill *et al.* (1970), described the results of 36 patients considered unsuitable for conventional treatment, 33 of whom had benign prostatic hypertrophy and 3, carcinoma of the prostate. The complications in this series included urinary tract infection, post-operative retention, incontinence and urethral stricture. In addition Green (1970), using this technique in 40 poor-risk patients, recorded an early mortality rate of 12·5 per cent.

The case to be described illustrates another hazard that can occur from this procedure.

CASE REPORT

A. D., a 67-year-old male was admitted on 25.2.70 with a 3 months' history of tiredness, lassitude, urinary frequency and polydipsia together with cramps in the hands and legs.

In 1968 he had been admitted with acute urinary retention to another hospital where the prostatic obstruction was treated by cryoprostatectomy. Five weeks following his discharge he was readmitted with acute urinary retention which was managed by the passage of bougies.

The patient's health prior to 1968 had been very good and he could not recollect having consulted his practitioner.

On examination he was slightly dehydrated, clinically anæmic and sallow in appearance. He had a moderate degree of hypertension 180/120 mm. Hg, basal crepitations and, on rectal examination, the prostate was very small.

Investigations on admission:

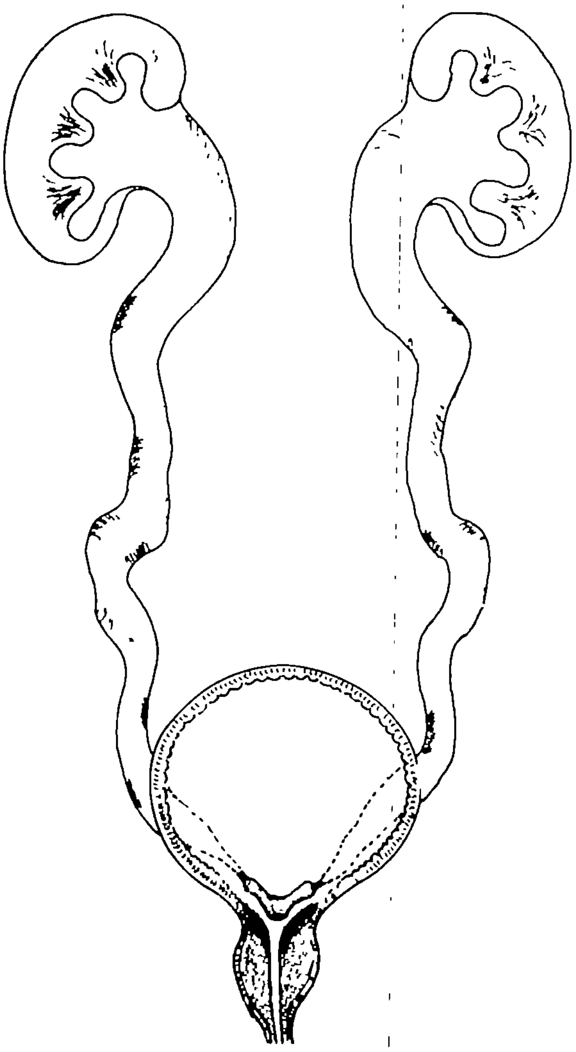
1.	Hb	7·4 g. per cent.
	WBC	5,400 cu. mm.
	ESR	13 mm./hr.
2.	Na	127 mEq./l.
	Cl	94 mEq./l.
	CO_2	19 mEq./l.
	Ca	3·65 mEq./l.
	Urea	294 mg. per cent.

3. Chest X-ray. The heart was moderately enlarged.
Small effusions were present at the costophrenic angles.

4. Urine Culture: no growth.
5. Blood Culture: no growth.

Intravenous urography was not done at this stage nor subsequently because of the elevated blood urea.

In spite of conservative management the blood urea rose rapidly to 486 mg. per cent. At this stage the patient underwent peritoneal dialysis and the blood urea fell to 148 mg. per cent.



Fibrosis of the trigone causing ureteric obstruction.

With this initial improvement it was decided to do a cystoscopy under local anæsthesia. The bladder capacity was found to be reduced to 100 c.c. and the entire bladder base involved in a fibrous process which also included the lower ureters. A cavity was also seen behind and involving the upper lateral prostatic lobes which were otherwise intact. The ureteric orifices could not be seen and therefore retrograde catheterisation was not even attempted.

From these findings it seemed likely that cryosurgery had involved the upper part of the prostate, the bladder base and probably the intramural ureters.

On 12.3.71 bilateral " T "-tube ureterostomies were made by muscle-splitting incisions through the iliac fossæ. On both sides the ureters were found to be grossly dilated and tortuous at the level of the pelvic brim. The subsequent progress was satisfactory, although the blood urea never fell below 136 mg. per cent.

In view of the marked symptomatic improvement it was decided that the lower ureters should be explored and if possible re-implanted into the bladder.

Six weeks later a laparotomy was done through a lower midline incision. The cystoscopic finding of fibrosis involving the bladder base was confirmed. Both ureters were then re-implanted into the bladder over portex tubing, extending proximal to the ureterostomy incisions and sutured distally to a suprapubic catheter. An indwelling urethral catheter was left in position.

The diagram shows the fibrous plaque which involved the trigone and base of the bladder and which also obstructed the ureteric orifices causing dilatation of the ureters and renal pelves.

Histology of the resected ureters confirmed their marked narrowing with replacement of the muscle layers by fibrous tissue.

The patient made an uneventful recovery and within 3 weeks of re-implantation micturition and continence were entirely satisfactory, although as expected the patient had polyuria. The patient was subsequently discharged with a sterile urine and a blood urea of 120 mg. per cent, which was undoubtedly due to irreversible renal destruction.

Regular out-patient follow-up was uneventful, but 6 months after operation he developed a further episode of acute retention and the blood urea rose to 330 mg. per cent. In spite of conservative measures to control this he died within 36 hours of admission.

CONCLUSION

The place of cryoprostatectomy in the management of prostatic obstruction is dubious. Its main application would seem to be in cases with severe cardio-pulmonary disease.

Its complications, however, particularly with inaccurate localisation of the cryoprobe, may be dangerous. In the case quoted here irreparable damage was sustained to the lower ends of the ureters causing progressive obstruction and resulting in chronic renal failure.

SUMMARY

A complication of cryoprostatectomy is described in which a patient presented with chronic renal failure due to obstruction at the lower ends of both ureters.

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BOOK REVIEWS

The Biochemical Consequences of Chronic Renal Failure. 1st Edition. By M. R. WILLS, M.D., M.R.C.Path. Pp. 218, with 9 figures. Aylesbury, England: Harvey Miller and Medcalf Limited. 1971. £3.

This is an interesting review of the biochemical changes in renal failure, particularly those chapters dealing with divalent ion metabolism. As an introduction the author considers the evolution of the kidney as an homeostatic organ and then goes on to mention the well known lack of toxicity of urea and to discuss the rôle of other metabolites in the production of the clinical features of uræmia. The rôle of acidosis is discussed, including its relationship to bone disease and then follows an extensive discussion of the inter-relationships of Calcium, Phosphorus and Magnesium metabolism. Alterations in Sodium and water handling are discussed with particular reference to the ætiology of hypertension in renal failure. In the concluding chapters, carbohydrate, lipid and protein metabolism are discussed, together with an account of some of the alterations in hormonal balance which occur. There is a very comprehensive list of recent references and the book presents an interesting insight into a field which is still full of unsolved problems. D. J. R.

Uremia: Progress in Pathophysiology and Treatment. 1st Edition. By JOHN P. MERRILL and CONSTANTINE L. HAMPERS. Pp. 115, with 30 illustration. London: William Heinemann Medical Books Ltd. 1971. £3·15.

This book brings together recent observations on the pathophysiology and treatment of uræmia and in doing so gives a concise and readable account of recent thinking on the important features of the uræmic syndrome. The book is divided basically into 2 sections: pathophysiology and treatment. The section on treatment gives a balanced account of current attitudes; of particular interest is the section on the management of renal osteodystrophy. Although the book makes no claim to being comprehensive, it does, nevertheless, give a broad view of the subject, particularly for somebody requiring an introduction. It's usefulness in this direction is enhanced by a very extensive list of references. D. J. R.

Ureterdynamik. Ed. W. LUTZEYER and H. MELCHIOR. Pp. viii+150 with 95 illustrations. Stuttgart: Georg Thieme Verlag. 1971. DM. 38.

This short paperback contains the proceedings of a symposium on ureteric function held in December 1969 in Aachen. The whole text is in German. The numerous contributions, all from Europe, cover many aspects of the ureter from its embryology, physiology and anatomy to the pathological states of refluxing and obstructed megaureters. There is the usual chapter showing that the ureter is resistant to the action of most drugs except adrenalin and Noradrenalin. There are extensive reports of electromyographic and manometeric studies which although adding to the understanding of ureteric function have little clinical applicability. A section on peristaltic models is strewn with apparently incomprehensible mathematical formulæ.

An analysis of 50 cases of primary obstructed ureter by W. Gregoir and G. Debled confirmed that the obstruction is not of neurogenic origin. Histologically, there was abnormal alignment of the muscle bundles and replacement by connective tissue in the terminal portion. Little practical advice was forthcoming as to when and whether these ureters should be reimplanted or tapered.

There was a final interesting section on the subtotal replacement of the ureter by a very long Boari flap.

It is reasonable to suppose that urodynamic studies are extremely relevant to the clinical investigation of the dilated ureter but it is disappointing to see that per-ureteric techniques are still being pursued. It is time that we measured directly the pressures in the renal pelvis where the deleterious pressure effects are taking place.

A short résumé of each section in English would have made this a more widely appreciated book.

R. H. W.

ABSTRACTS OF THE PROCEEDINGS OF THE UROLOGICAL SOCIETY OF AUSTRALASIA

TWENTY-FIFTH ANNUAL GENERAL MEETING, SURFERS PARADISE, 1972

President: J. G. WATSON (Brisbane)
Honorary Secretary: G. R. GIBSON (Sydney)
Editor: G. F. Murnaghan (Sydney)

Some Observations on Ureteric Anomalies

By R. A. MOGG, V.R.D., M.Ch., F.R.C.S.

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Ureteric anomalies have always proved to be a fascinating study. The diversity and complexities of these anomalies may produce a most bizarre clinical picture; with ureteric ectopia differences in symptomatology may relate to wide variety in the site of ectopic termination in the two sexes. In the male the ectopic ureter may terminate in the prostatic urethra (54%), the seminal vesicle (28%), vas deferens (10%) or the ejaculatory ducts (8%), whereas in the female the most common site is in the vestibule (38%), less commonly in the urethra (32%), the vagina (27%) and the uterus (23%).

Urinary incontinence may result from the ectopic opening of the ureter into the urethra but may also be related to an abnormal bladder neck mechanism. There is a variable incidence of reflux and ureterocele and a secondary reflux may also be encountered if such obstructive lesions as bladder neck stenosis and megacystis are also present.

Pyelographic diagnosis of ureteric duplication may be elusive and cysto-urethrography may not always reveal the orifice of the ectopic ureter. It may be extremely difficult to determine the site of a stenotic ectopic ureteric termination, whereas micturating cysto-urethrography may provide valuable information in that large proportion of cases of ectopic ureter or ureterocele allowing reflux into the ectopic ureter.

In the majority of cases of ectopic ureteric termination, definitive treatment is applied by partial nephrectomy combined with ureterectomy. If both renal elements of any duplication show functional impairment, then total nephro-ureterectomy must be carried out. Whenever possible, the lower urinary tract should be explored in the first instance; the procedure may develop to partial uretero-nephrectomy if the condition of the child permits. Otherwise a cutaneous ureterostomy is employed to drain the anomolous upper urinary tract to allow for definitive surgery to be performed on the lower portion of the ectopic ureter, with subsequent later partial nephrectomy and removal of the remaining upper ureter.

End-to-End Uretero-Ileal Anastomosis in the Formation of an Ileal Conduit

By P. CLARK, M.A., M.D., M.Chir., M.B., B.Chir., F.R.C.S.

General Infirmary, Leeds, England

Since 1964, in a personal series of 50 patients, the formation of an ileal conduit has included the anastomosis of the ends of both ureters side-to-side to form a single ureter which has been anastomosed end-to-end into the ileal conduit. The aim of this procedure has been to form a simple Y junction possessing a normal peristalsis between the ureters and the conduit.

This group of patients has been assessed by tests of renal function, pyelography and pressure studies in the conduit. Stenosis of the uretero-ileal junction has been rare and renal function has remained excellent in the majority of patients.

An Experimental Study of Ureteric Dynamics after Uretero-Colic Anastomosis

By G. F. MURNAGHAN, M.D., Ch.M., F.R.C.S.

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After preliminary dynamic and histological studies of the normal dog ureter, uretero-colic anastomosis was carried out in a series of 33 dogs using different ureteric levels of implantation and different techniques of surgical anastomosis. After survival periods up to 40 weeks the animals were subjected to laparotomy to allow for visual studies of ureteric calibre and contractility, prior to perfusion of excised nephro-uretero-colic segments *in vitro* so that any stenosis or reflux at the anastomoses would be detected and graded. Transverse sections of the uretero-colic specimens were subsequently prepared for histology and the different proportions of circular, long and oblique bundles of muscles were assessed as areas in each transverse section by projection drawing with planimetry.

These experimental studies showed that the dog ureter usually responds to uretero-colic anastomosis by some degree of hypertrophy so that strong normal contractility of the ureter can be maintained and may persist for prolonged periods despite anastomotic stenosis or incompetence. After uretero-colic anastomosis, hydro-ureter will develop easily and obviously as the result of stenosis or incompetence of the anastomosis and in association with increased predominance of longitudinal muscular hypertrophy in the ureteric wall adjacent to the anastomosis with the colon.

Marked dilatation of the collecting system and ureter may also develop without stenosis or reflux at the uretero-colic anastomosis but in association with retrograde ureteric contractions. Such abnormal ureteric dynamics are associated with a redistribution of the ureteric muscle fibres in a circular direction analagous to the pattern described in human primary mega-ureter. These structural and dynamic changes were found to occur without regard to the level of the ureter which had been implanted into the colon.

Indications for Urinary Diversion in Children

By E. DURHAM SMITH, M.D., F.R.A.C.S., F.A.C.S.

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Most permanent diversions in children are elective decisions for social incontinence or because of the predictability of upper urinary damage, as in the neurogenic lesions or in ectopia vesicae and epispadias. Much less commonly the diversion becomes obligatory in order to save life as in the removal of pelvic malignancy or in an irretrievably dilated upper urinary tract.

1. *Neurogenic bladder disorder:* The need for urinary diversion commonly occurs in congenital spina bifida cystica and occulta, and sacral agenesis, but is uncommon in spinal trauma, tumour and infection and rare in cerebral palsy. Previously a conservative policy of management was adopted, provided that the child was clinically well and the upper urinary tract anatomically normal and uninfected; diversion was advocated if Crede bladder expression could not achieve at least two hours of dryness, or the upper tract showed objective evidence of deterioration (infection, dilatation, functional loss). Since 1965 a more radical approach has been adopted in the congenital lesions because of (*a*) the almost universal failure of conservative bladder training, with or without bladder or urethral operative procedures, in achieving social dryness; (*b*) penile appliances in males fail because of penile ulceration, leakage, infection and upper tract change; (*c*) infection occurs in over 90% of patients over two years of age; (*d*) there is a progressive deterioration of the upper urinary tract in more than half the patients over two years of age; (*e*) urinary diversion seldom reverses the renal risk if it is deferred until objective evidence of change in the upper urinary tract is apparent

In lesions with incontrovertible evidence of permanent neurogenic bladder disorder, urinary diversion is advocated early (at about two years of age or earlier in infected) while the upper urinary tract is still normal. As to the types of diversion, vesicostomy does not remove the risk of infection in the neurogenic bladder. Bilateral cutaneous ureterostomy is a simple procedure but is only applicable to mega-ureters because of the risk of stomal stenosis; it may not relieve the upper urinary stasis associated with very large mega-ureters. Ileal or colonic conduit diversion is the optimum method when the ureters are of normal calibre or show but mild dilatation. Pyelo-ileal conduit may be used for the relief of gross mega-ureter formation.

2. *Sacral agenesis:* Bladder innervation may be intact despite severe agenesis so that clinical evaluation of urinary incontinence rather than the radiological appearances of the sacrum should be the final arbiter in consideration of urinary diversion which is required by most patients with this spinal defect.

3. *Ectopia vesicae and epispadias:* Permanent urinary diversion is required when bladder and bladder neck closure has failed to provide continence or when closure is followed by dilatation in the upper urinary tract. In this condition the anal sphincters are intact so that urinary diversion into the colon is possible and especially if puborectalis function is improved by iliac osteotomy. Ureterosigmoidostomy is a feasible form of diversion if the upper urinary tract is anatomically normal and if regular pyelographic and biochemical reviews are available. When abnormality in the upper urinary tract develops following closure of the bladder or after ureterosigmoidostomy, then conversion to an ileal or colonic conduit is performed. Experience with the Lowsley-Johnson or Heitz-Boyer forms of diversion has been disappointing in children.

4. *Trauma:* The bladder or its sphincters may be damaged by penetrating external injury, or by internal nerve disruption during rectoplasty for imperforate rectum or Hirschsprung's disease.

5. *Malignancies:* Palliative ureterosigmoidostomy or permanent ileal conduit diversion is obligatory following extirpation of rhabdomyosarcoma of bladder, prostate, or pelvic adnexae and is occasionally required when haemorrhagic necrotic cystitis follows cytotoxic drug therapy.

6. *Gross upper urinary tract anomalies.* Although the primary attack on huge static mega-ureters is directed to the causative pathology (urethral valves, vesico-ureteric obstruction, ureteric reflux, triad syndrome, etc.) continued stasis and infection may be life-threatening, and permanent pyelo-ileal diversion may be obligatory.

These views are based upon experience of 225 children with permanent urinary diversion.

Complications of Urinary Diversion

By J. S. JOSE, M.B., B.S., F.R.A.C.S., F.R.C.S.

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During a review period of five years urinary diversion by uretero-ileal conduit has been performed upon a series of 47 patients, for the relief of the benign or malignant disease. Post-operative complications occurred in 19 patients (40%) and later complications developed in 23 patients (50%) but there were no post-operative deaths.

When urinary diversion is performed without cystectomy, then the operation is relatively uncomplicated, but pre-operative radiotherapy does significantly increase the complication rate.

Specific complications of the uretero-ileal diversion include anastomotic leakage which is hard to diagnose with certainty but which usually responds to conservative treatment. Anastomotic stenosis is relatively common as a late *sequela* but may cause either non-function of the corresponding kidney or increasing hydro-nephrosis. Such stenosis may be minimised by the practice of end-to-end uretero-ileal anastomosis. In two patients necrosis of the ileum may have been predisposed by pre-operative irradiation; careful selection of bowel segment based upon vascular arcades has ensured no other loss of the isolated intestinal·loop.

Intestinal obstruction has occurred in nine patients in the series as the result of intestinal adhesions. The isolated loop has not been involved in this process and no attempt has been made to obliterate the lateral peritoneal gutter. In five patients, there has been obstruction of the ileal conduit; in three patients this obstruction was due to stomal stenosis which can be avoided by evertion of the bowel on the abdominal wall; in the remaining two patients, conduit obstruction was associated with abdominal obesity.

Leakage of urine from collecting apparatus was often associated with poor siting of the stoma which should be constructed away from scars and in a site individually selected for each patient. One patient presented an allergic reaction to the urinary collecting apparatus.

Urinary Diversion in Cases of Meningomyelocele

By WARWICK MACKY, F.R.A.C.S.

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In November 1971, there were 92 cases of meningomyelocele registered in Auckland City, with a population of approximately 550,000 people. There were 47 females and 45 males. Over the past five years, an average of 14 new cases were added to the register per annum and an average of four patients died within the first few years of life.

Approximately 50% of the cases were less than six years of age, and four children who were born before 1960, when the Spitz-Holter valve for atrio-ventricular shunt was effectively introduced, are alive at the time of review.

If present policies of management are continued then the implications in terms of human suffering and socio-economic upheaval are daunting to contemplate.

In the general plan of management the spinal defect is usually closed at birth and a Spitz-Holter valve is inserted within a few weeks after closure if hydrocephalus develops. On registration at the co-ordinating clinic, supervision by various specialists and district visiting nurses is arranged.

Urological review is arranged at the age of a few months in order to detect and treat urinary tract infection, to assess renal function and to determine the type of neurogenic bladder disorder. Conservative management with regular Crede expression of the bladder is implemented at this stage and the implications of urinary diversion are discussed with the parents.

In general, ileal conduit diversion before school age is strongly favoured but case selection and timing should be individually assessed with due regard to intellect, associated deformities, home conditions and respect for the parents' viewpoint.

Cutaneous ureterostomy was carried out in six patients (three female and three male) but in four patients the diversion has subsequently been converted to ileal conduit because of problems of stomal contraction and retraction and difficulties with collecting apparatus.

In 25 pateints uretero-ileostomy has been carried out (15 female and 10 male) at an average age at operation of 5·5 years but with an age range from 20 months to 14 years. These procedures have been accomplished without mortality and with low morbidity.

Early complications of ileal conduit have included one case of intestinal obstruction due to volvulus. One severe haemorrhage from the ileal stoma; six patients had electrolyte disturbance; 12 patients had a transient urinary leakage with peritonitis and ileus; 12 patients had severe early skin reaction around the stoma.

Amongst the late complications there were four instances of pyocystis, two of which required cystectomy. Stomal ulceration with bleeding and encrustation occurred in two patients and one patient had late rupture of the conduit with severe peritonitis.

A programme for the eduction of patients and ancillary workers in the management of ileostomy must be enthusiastically promoted and the search for better collecting devices must be diligently pursued.

Urethroplasty

By J. L. WILLIAMS, M.B., B.S., F.R.C.S.
B. S. CRAWFORD, M.B., Ch.B., F.R.C.S.

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The treatment of urethral strictures by dilatation is not always possible and may result in severe complications. In such patients, a two-stage method of urethroplasty has been carried out utilising a scrotal flap. The urethra is opened through the stricture into normal proximal urethra and the flap is sutured to the normal urethral epithelium proximal to the stricture, to leave the patient with a scrotal or perineal hypospadias. The second stage of the operation uses the buried-strip principle to close the hypospadias.

Since 1964, 85 patients have undergone this urethroplasty, whilst three patients have been treated by end-to-end urethral anastomosis with good results. The commonest site of stricture was in the bulbous portion of urethra and though the age incidence varied from 10 to 75 years, the highest incidence occurred in the 40-65 age group; 45 patients have had both stages of the urethroplasty completed and 19 are awaiting the second stage of the procedure. Twelve patients have refused to undergo the second stage because they are quite content with urethral function through the hypospadias; in nine patients the second stage is not contemplated because of technical reasons.

The Conservative Management of Urethral Stricture

By G. R. Gibson, LL.B., F.R.C.S., F.R.A.C.S.

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Sixty-two patients with urethral stricture have been treated by regular dilatation during the nine year period 1963-1971. The purpose of the urethral dilatation is to stretch the peri-urethral scar tissue without inducing rupture of the epithelium, bleeding and the possibility of further scar formation. Ability to dilate the stricture to size 10/13 (Lister) at intervals of three months or longer, was considered to be a good result of this management; more frequent dilatation, smaller calibre, repeated infection or bleeding required a classification of the result as fair, whilst frequent infection, pain, tight structures and bacteraemia allowed for classification as a poor result.

Twenty-one patients with previous gonococcal urethritis presented for review with an average age of 70 years and an average duration of stricture of 27·5 years. No recent post-gonorrhoeal strictures have been seen. Of the 21 patients, 18 have had a good result from conservative management and one a fair result. Two patients in this group showed a poor response and both died after septicaemia as a result of urethral instrumentation.

Fifteen patients had post-traumatic strictures of the urethra following fracture of the pelvis with rupture of the membranous urethra in 11 patients and following astride injury to the bulbar urethra in four patients. The results of conservative management were good in 12 patients, fair in two patients and poor in one patient in this group.

Twenty-six patients comprised the post-operative group with strictures following transurethral prostatic resection in 18 patients, open prostatectomy in four patients and various other urological procedures in the remaining six patients. Stricture formation appeared to follow resection of small prostates (average weight of 12 g.) whilst fibrosis of the prostate was commonly identified in both the resection and enucleation groups of post-operative strictures. Regular urethral dilatation had a good result in 23 patients and a fair result in two and a poor result in one patient with a tight stricture requiring monthly instrumentation.

In the entire series, satisfactory control was achieved in 53 of the 62 patients (85%). Infection occurred sometimes in 12 patients and was serious in four and led to the death of two patients. Bleeding was not common. Urinary retention occurred early in the period of treatment. Internal urethrotomy was included in the management of nine patients and open excision of the stricture was required in three patients of the post-traumatic group. In each of the patients requiring operative treatment, some degree of urethral stricture remained but was amenable to post-operative urethral dilation.

Most patients with urethral stricture, from whatever cause, can be managed by regular dilatation.

Congenital Urethral Strictures

By A. P. Tynan, F.R.C.S., F.R.A.C.S.

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Apart from stenosis of the external urethral meatus, urethral obstruction in early life is almost always due to posterior urethral valve formation. Congenital "stricture" in the anterior urethra is usually associated with some form of urethral duplication or mucosal valve or diverticulum formation.

Symptomatology may be bizarre and a clinical diagnosis may not be made in early life and may elude routine urological examination but be manifest on careful radiological study.

A four-year-old boy presented with a life-long history of marked diminution of the urinary stream with diurnal and nocturnal incontinence of urine. No evidence of posterior urethral valve was obtained and the urethra could be calibrated to quite large size by antegrade and retrograde instrumentation. A combination of voiding and ascending cysto-urethrography demonstrated a spiral defect in the anterior urethra which was confirmed at urethrotomy to derive from anterior spiral urethral valve formation.

A five-year-old boy presented with hæmaturia without any difficulty with micturition or diminution of the urinary stream. Passage of any instrument through the normal urethral meatus on glans penis was obstructed in the navicular fossa. More careful examination of the frenulum revealed the hidden meatus of a wide calibre urethra through which easy micturition could occur. The anterior channel of his complete urethral duplication terminated normally on the glans penis but was of extremely fine calibre and could not be negotiated by any instrument.

The third patient presented at the age of 17 months with right-sided epididymitis. The right scrotum had been explored on the mistaken diagnosis of recurrent testicular torsion. Whilst in hospital, it was observed that the patient dribbled urine from a small fleshy papilla immediately anterior to the anal margin, in addition to urine discharge from the external meatus on the glans penis. His mother confirmed that he had always "wet his nappies behind as well as in front". Cysto-urethrography demonstrated extreme narrowing of the anterior urethra with marked dilatation of the posterior urethra and with a narrow perineal duplex urethra extending as a fistula from the prostatic portion down to the perineal papilla.

Current concepts of the embryology of the urethra could explain anterior urethral duplication by double tubular closure of the urethral groove in a manner analogous to duplication of the gut. Incomplete closure of the urogenital sinus would allow for the development of perineal urethral duplication but there is no clear explanation for the derivation of anterior urethral valves.

Complications of Circumcision

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Complications of circumcision are usually related to haemorrhage, infection or surgical tissue loss.

Haemorrhage may be due to inadequate haemostasis, blood coagulation defects or anomalous penile vessels.

Infection of the circumcision wound is fairly common and occasionally may lead to septicaemia or to necrosis of the penis. Less severe infection may produce contraction and fibrosis of the circular wound or may be associated with meatal stenosis. Occasionally fistula formation follows penetration of a deep haemostatic suture into the urethra at a site just proximal to the frenulum.

Undue or unusual loss of tissue is due to simple excessive excision, sometimes amounting to accidental amputation of the penis. Other variations include accidental laceration of penile or scrotal skin and incomplete circumcision.

The rather formidable list of complications requires review of circumcision regarding its place in preventive medicine with particular regard to tumours of the penis, cervix or prostate and with regard to venereal infection. Carcinoma of the penis has a higher incidence in the uncircumcised but the influence of retention of smegma with poor hygiene remains obscure. Animal experiments with monkeys have failed to prove that smegma is carcinogenic to the cervix. Comparative studies undertaken in Sweden and Israel have thrown doubt upon any influence that circumcision might have upon the incidence of prostatic carcinoma.

Venereal disease in the event is more common in the lower socio-economic groups where circumcision is not routinely applied.

The ultimate practice of personal hygiene is probably the decisive factor in evaluation of the contention that routine circumcision may prevent more problems than it creates.

Vesical Bilharziasis

By R. Parisi, F.R.C.S.(Glas.), F.R.C.S.(Ed.), F.R.A.C.S.

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Vesical bilharziasis is a parasitic disease generally caused by the fluke *Schistosoma haematobium*. It was recognised in ancient times but it is rare in Australia. The diagnosis should be considered in any visitor from a high-incidence area, who presents with low-grade fever, localised urticarial reaction, respiratory or gastro-intestinal disturbances, irritable bladder symptoms or haematuria.

Diagnosis is established by the finding of typical ova in urine or faeces or by endoscopic examination and biopsy of the bladder. Treatment is largely medical and 80% cure rates have been reported following the intramuscular administration of antimony salts or oral medication with niridazole, but surgical treatment may be required for late irreversible complications such as ureteric stricture, bladder contracture, calculus or tumour, urethral sticture of peri-urethral abscess.

A twenty-year-old male Ghanaian, studying in Townsville, presented with terminal haematuria of four weeks' duration. His urine was sterile on culture and his excretory pyelograms were normal in appearance. Cystoscopic examination revealed small yellow granules with larger greyish nodules, raspberry granulomata and shallow ulcers in the bladder mucosa. Biopsy demonstrated ova with terminal spines morphologically resembling *Schistosoma haematobium* and also demonstrated pseudotubercle formation. Ova were not found in urine samples.

The haematuria resolved after a seven-day course of oral treatment with niridazole (25 mg./kilo/day) which was accomplished without side effects.

Transvesical Prostatectomy

By W. Selby Tulloch, F.R.C.S.(Ed)

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Following an historical survey of transvesical prostatectomy with some review of the studies of the surgical pathology of prostatectomy carried out by Henry Wade in Edinburgh (1910-1912), the many advantages of the transvesical approach were emphasised.

The transvesical approach is quick, direct and safe and can be applied to " prostatectomy " without the insertion of sutures or the application of diathermy to the operative field in the prostatic area. Haemostasis may be obtained by a gentle tamponade of the prostatic cavity with a balloon urethral catheter through which sterile saline irrigation may be provided to the bladder and cleared by suprapubic sump drainage through a modified Stedman tube.

This method has proved most quick and efficacious in patients who constitute a significant surgical risk because of age, debility or concurrent pathology in other systems.

Results of Vasal Anastomosis following Voluntary Vasectomy

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Vasectomy is now an established form of male sterilisation in Britain and is accepted on ethical and clinical standards by a majority of people. It is a relatively simple and relatively safe procedure but is associated with a very definite but low morbidity rate.

Many individuals and some of the official bodies in Britain assume that vasectomy is irreversible and make quite sure that the " couples " are informed of this fact and may argue that this dogmatic approach is a psychological stabilising factor. However, vasectomy is not necessarily irreversible but the success rate following re-anastomosis of the vas is almost entirely dependent on the manner in which the original vasectomy was performed. Success is inversely proportional to the amount of vas removed and the subsequent haemorrhage and inflammatory reaction which develops.

Re-anastomosis has not been attempted unless both ends of the vas in the scrotum can be palpated. Re-anastomosis was technically satisfactory in 35 patients, in three of whom the sutures were under some tension owing to a rather long defect but in 32 patients the conditions were optimum. Motile spermatozoa were detected in the testicular ends of the vasa in all but one instance. Sperms appeared in the ejaculate in 27 of the 35 patients (77%) and in useful numbers above 20 million per ml. in all but three of the men.

Out of 27 technical successes there were only eight pregnancies going to full term and two abortions occurred with one other "couple". Sperms will appear in the ejaculate in well over 50% of cases but for various reasons, there is no guarantee that pregnancy will ensue and in the presence of sperms, the eventual conception rate was 33%.

Agenesis of the Abdominal Musculature

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This is a rare anomaly, yet a most intriguing condition. The basic syndrome comprises partial or complete deficiency of the lower abdominal muscles, with manifestations of obstructive uropathy of the lower urinary tract which are often associated with dysplasia of the renal element. Genital lesions and associated lesions of the gastro-intestinal and skeletal systems are encountered. The condition is essentially confined to males and in the newborn infant it is typified by protuberance of the umbilicus with lax abdominal musculature with wrinkling of the skin of the abdominal wall.

The bladder is always of large capacity. Umbilical fistula is common and the posterior urethra is widely dilated despite the absence of any obvious cause for this malformation. The kidneys are hydro-nephrotic and dysplastic with gross dilatation and tortuosity of the ureters with evidence of excessive fibrosis in their walls. Death is frequently due to renal failure with or without renal infection.

Some of the features of the so-called "Triad Syndrome" presented in a patient stylised as a "pseudo-prune". This 22-year-old male patient was first seen at the age of three and a half years with partial agenesis of the muscles of the anterior abdominal wall, more marked on the left side and associated with non-descent of the left testis. Pyelography showed bilateral hydro-nephrosis with grossly dilated tortuous ureters. The bladder was clinically distended. Further investigations of the urinary tract were not performed because the child was free from symptoms. He remained well but further pyelography was carried out at the age of 19 years and this showed well-marked right hydro-nephrosis to be associated with vesico-ureteric reflux, possibly with pelvi-ureteric obstruction. After micturition there was retention of contrast within the ureters and the bladder, possibly associated with vesico-ureteric reflux. Further treatment and correction of any reflux with surgical revision of the upper urinary tract may be needed but this patient with the incomplete syndrome is reluctant to undergo any form of surgical treatment whilst he remains symptom free and in perfect health.

A Simple Operation for the Treatment of the Large Non-ectopic Ureterocele

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Ureterocele is a congenital deformity producing an intravesical ballooning of the dilated submucosal ureter. When the site of ureteric termination is orthotopic, a wide range of treatment in available within the range of simple observation to complete nephro-ureterectomy according to the size of the ureterocele, preservation of ureteric peristalsis and the quality of renal function. Most non-ectopic ureteroceles can be treated by minor enlargement of the ureteric orifice as an endoscopic procedure.

For those patients presenting with ureterocele of sufficient size to require treatment by open operation, a simple procedure has been devised which prevents subsequent vesico-ureteric reflux without the need for ureteric reimplantation. Similar techniques have been described by other workers with the same objective of prevention of reflux without the necessity for the more major procedure of ureteric reimplantation with its possible complications.

With this technique, the bladder is opened and the limits of the ureterocele are defined. Traction is exerted on the ureterocele and the roof is excised. At this stage it is advisable to leave an adequate amount of the side wall of the ureterocele which may be trimmed at a later stage. If the bladder wall is weak then it can be buttressed behind the ureterocele.

The two layers of the ureterocele are thus obvious and can be further separated by gentle dissection. In adult patients a 10F size catheter is passed into the upper ureter; the layers of the ureterocele are then trimmed. The first layer is closed over the splint catheter with continuous 4/0 chromic catgut, the second layer is then closed in a similar manner and in a watertight fashion. The splint catheter ensures an adequate lumen; the length of the submucosal tunnel which has been constructed serves to prevent reflux.

The ureteric splint catheter is removed and a profuse diuresis is induced by the intravenous administration of Lasix. Deliberate obstruction of the ureteric orifice then allows for observation of leakage through the suture line which may then be reinforced. The bladder is closed with a watertight purse-string suture and without drainage.

Autotransplantation of the Kidney

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Although a number of reconstructive procedures are now available for the surgical relief of hypertension due to renal artery stenosis, they have all been associated with a significant incidence of post-operative thrombotic complications, so that nephrectomy has frequently been required as a secondary procedure. Where the nature or site of the original vascular lesion is such that by-pass or reconstruction are not easily carried out, and the only alternative is nephrectomy, then autotransplantation of the affected kidney by anastomosis to the iliac vessels should be considered.

In March 1969, such renal autotransplant was carried out in a young woman suffering from severe hypertension associated with fibro-muscular hyperplasia of the right renal artery with the disease process extending beyond the bifurcation of the artery. This patient remains well and is normotensive for more than three years after operation.

A second female patient with similar clinical features was treated by the same operative procedure in February 1970. She has shown a gradual improvement in blood pressure control until she is now normotensive without further drug therapy.

In a third patient, a boy of 14 years of age, re-implantation of a stenosed left renal artery into the aorta in March 1970 was followed by thrombosis of the main renal artery with extension of the thrombus to the bifurcation; there was recrudescence of severe hypertension. This became completely controlled after autotransplantation of the left kidney.

The fourth patient, a man of 60 years of age, had been known to have mild hypertension for some years, and in December 1970, developed malignant hypertension and intravenous pyelography then failed to demonstrate evidence of function in a small right kidney. Function of the left kidney was also poor and arteriography demonstrated diffuse atheromatous change with complete occlusion of the right renal artery at its origin from the aorta. It was felt to be essential to attempt to restore some function to the right kidney. At operation it was found that the right renal artery was occluded with atheroma and thrombosis had extended up to the bifurcation of the artery; renal autotransplantation was carried out and has been followed by return of good function in the transplanted kidney. The hypertension is now easily controlled by medical means.

In these four patients, autotransplantation of the kidney has proved to be a valuable alternative to the routine methods of renovascular reconstruction. The procedure has proved to be so satisfactory that it has recently been applied to the operative treatment of circumscribed fibro-muscular hyperplasia of the right renal artery in two female patients with the consequent control of their pre-operative hypertension.

It is suggested that autotransplantation of the kidney could in fact be the operative procedure of choice in patients suffering from hypertension due to renovascular disease, particularly in those patients with lesions affecting the right renal artery.

Analgesic Nephropathy with Renal Failure—Surgical Aspects

By Warren Johnson, F.R.A.C.S.

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A group of 45 patients who have been admitted to hospital with renal failure thought to be due to abuse of analgesic drugs has been studied during an average follow-up period of 28 months.

In each patient, serum creatinine level was in excess of 4 mg. %.

A diagnosis of renal papillary necrosis has been based upon a history of analgesic abuse, radiologic features, histological study of voided papillary material, renal biopsy or the pathological examination of a kidney at autopsy or after nephrectomy.

In the series there were 30 female patients and 15 male patients with an average of 53 years and the youngest patient was 34 years of age. The patients presented most commonly, with symptoms of uraemia (23) but flank pain (ten) and urinary infection (four) were also common. Less common presentations included gross haematuria, anaemia, anuria, and hypertension as an incidental finding.

Ninety-five per cent of the patients had pyuria, and 85% had microscopic haematuria. Urinary infection was extremely common and was usually recurrent. At the initial presentation the average serum creatinine level was 9·8 mg. %.

Retrograde pyelography was carried out on 54 occasions in 44 patients. Renal papillary necrosis was demonstrated in 29 studies, obstructing papillae in 11, separated papillae without obstruction in eight, calcification in papillae in four, whilst two studies were considered to be normal.

It has been considered that surgical treatment was indicated for the relief of obstruction, free papillae with chronic infection, free papillae which were too large to pass spontaneously and pyonephrosis. A total of 16 operations have been carried out on 13 patients in the series, the procedures included, pyelolithotomy and nephrostomy (six), endoscopic extraction of ureteric papillae (four), pyelolithotomy (three), nephrectomy (two), pyelo-ureterolithotomy and nephrostomy (one).

Each patient has received intensive medical treatment with avoidance of further analgesic intake.

Twenty-eight patients in the entire series showed clinical improvement but two did not improve. Fifteen patients died and death was attributed to ischaemic heart disease in six, to septicaemia in three, to uraemia in three, to cerebro-vascular accident in two and to unrelated causes in one patient.

Subsequent follow-up has shown that significant deterioration has occurred in only two of the 28 surviving patients who were improved initially.

Progress with Jejunal Loop Dialysis

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The incidence of chronic renal disease in Queensland's country areas (2·2 to 3·7/1000) is higher than that in Brisbane (1·8/1000). The number of cases presently treated in Queensland by dialysis or dialysis and renal transplantation is less than half the number to be expected from the population and there is an urgent need for extension of dialysis services outside Brisbane.

Since 1968 ten patients, of whom five were male and five were female, have been treated in Townsville by isolated jejunal loop dialysis. The age range extended from 27 to 62 years and each patient was grossly anaemic; nine patients had severe hypertension which was poorly controlled in eight and seven patients had been rejected from dialysis treatment in other centres. Five patients had chronic pyelonephritis, four had polycystic kidneys and one had chronic glomerulonephritis. Six patients had creatinine clearance values of 0 to 3 ml. per minute; three patients of 3 to 5 ml. per minute and one patient a clearance value of 7 ml. per minute.

No operative mortality accompanied the procedure but ten patients experienced a mild abdominal cramping; five patients had mild blood staining of the effluent; four patients had retrograde intussusception of the proximal stoma; one patient had a " burst abdomen ". Some hypernatraemia and metabolic alkalosis occurred but is usually avoidable.

Three patients are alive at 48, 12 and 9 months with respective creatinine clearances of 7, 2·9 and 2·8 ml. per minute. Seven patients survived for periods between one and seven months after the commencement of dialysis and four of these died from cardio-vascular complications despite peritoneal dialysis. One died of hypertensive encephalopathy precipitated by hypernatraemia but only one patient died of uncontrolled renal failure because haemodialysis was not available and peritoneal dialysis was not feasible.

During dialysis an isolated 6 ft. loop of proximal jejunum is perfused with fluid at body temperature at a flow rate of 2 l. per hour. Composition of the fluid varies according to individual patient needs. The solution must be hyperosmolar and is made up from tap water, sucrose, salt sodium bicarbonate and effervescent potassium tablets. Sodium and bicarbonate are actively absorbed but potassium exchange occurs by simple diffusion.

Use of jejunal loop dialysis at home has offered excellent control of water balance, potassium and sodium levels and acid-base balance without restrictions and with acceptable haemoglobin levels without blood transfusion. Elevation of serum inorganic phosphate levels has been slowed but has not been prevented and oral aluminium hydroxide has been required for levels reaching 9 mgm. %. Hypertension was controlled in seven patients without specific medication but there was no response in two patients because of high renin levels.

With the possible exception of urea, the excretion of nitrogenous waste products may be inadequate and serum levels will rise in indirect proportions to the amount of residual renal function. Uric acid levels can be controlled with allopurinol. High levels of creatinine or guanidines may require correction by occasional peritoneal or haemodialysis.

All patients with chronic renal failure have been found to have elevated levels of serum total indoxyl ester (normal range 0·08 to 0·5 mgm./100 ml) in proportion to the severity and chronicity of the renal failure. Qualitative serum indoxyl glucuronide levels appeared to demonstrate a close correlation with the patient's clinical condition and it is suggested that indoxyl glucuronide could be a major uraemic toxin responsible for neurotoxic manifestations which are largely reversible. Oral lactulose and lactobacillus have been used with some success to reduce intestinal production of indoles with limitation of serum ester levels.

Jejunal loop dialysis is considered to be a satisfactory alternative to restriction of intake of protein, water and electrolytes; it aids the control of hypertension with some preservation of any existing renal function; it may be used in combination with interval haemodialysis with corresponding reduction in cost and personnel with extension of the availability of dialysis treatment.

This technique forms a useful research instrument for the study of intestinal transport mechanism and the chemical control of toxins. Future research projects include the chemical alteration of loop membrane to improve clearances, the use of disposable or rechargeable selective absorption mini-dialysers in conjunction with jejunal loop dialysis for the selective control of water and electrolyte-levels. It is hoped that the technique of loop isolation will be refined to reduce the incidence of intussusception whilst improvement of the apparatus may ultimately allow for unsupervised dialysis during sleep.

Bilateral Nephrectomy for Malignant Hypertension

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During the past three years nine patients have been subjected to bilateral nephrectomy because of drug-resistant malignant hypertension. Each patient had progressive renal failure with recent retinal haemorrhages and exudates and eight of the nine patients had papilloedema. In eight of the patients the underlying disease was essential hypertension whilst the ninth patient had chronic pyelonephritis.

Each patient was treated with dietary sodium restriction and anti-hypertensive drugs; each had been given dizoxide at least once; five of the nine patients required nitroprusside infusions. Each patient had also been given a trial by dialysis. In seven of the nine, hypertension rather than azotaemia was the prime indication for dialysis.

Plasma renin levels were found to be significantly elevated in each of the five patients tested. Prior to nephrectomy all patients were accepted for haemodialysis and for subsequent renal transplantation.

In six patients nephrectomy was performed using a loin approach and a transverse abdominal incision was used in the remaining three patients. One patient sustained a burst abdominal wound requiring resuture.

In each of the nine patients the diastolic blood pressure fell after nephrectomy and in seven of the nine patients was down to a level of 90 mm. of mercury or less by the first post-operative day. The mean (± S.E.M.) systolic blood pressure was 211 (± 6·0) mm. of mercury immediately before operation; one day after operation the mean systolic pressure was 140 ± 7·3) mm. of mercury and the diastolic pressure 92 (± 5·1) mm. of mercury. Fall in both systolic and diastolic pressures was significant (P > 0·001).

One patient died from septicaemia one week after operation, but the remaining eight were available for follow-up periods up to 13 months. Two patients remaining on haemodialysis have not required anti-hypertensive therapy. Six patients have received cadaveric grafts, one of which did not function at any stage and the blood pressure of this patient was controlled by dialysis for a period of ten months until death resulted from hyperkalaemia. Another patient died from cerebral thrombosis occurring nine months after kidney transplantation. Four patients who received kidney grafts are alive with functioning grafts; three of these four patients have required drug therapy for the satisfactory control of blood pressure.

Drug resistant malignant hypertension carries a poor prognosis so that bilateral nephrectomy may be necessary to preserve vision and allow for subsequent control of hypertension.

Stress Haematuria

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Contrary to expectation, persons engaged in contact sports such as cycling, horse-riding, sculling and boxing do not produce an increase in red cell excretion in their urine. Such haematuria with exercise has been noted in persons engaged in running sports or subjected to acceleration forces in the upright position.

It is thought that increase in renal vein pressure as the result of kinking of the vein at its junction with the inferior vena cava may be followed by diapedesis of red blood cells into the lumen of the upper urinary tract. The left renal vein is far longer than the right and bleeding is seen to issue from the left ureter with twice the frequency of right-sided bleeding.

Long-distance runners have been investigated and have been found to have an appreciable rise in red cell count in urine collected after racing; in contrast both initial and mid-stream urine samples collected after a 120-mile bicycle race rarely show any rise in red cell content. Many athletes are lean and may not have a large amount of peri-renal fat so that the kidneys are likely to descend significantly during the continuous stamping action of a runner or long-distance walker so that the angle between the renal veins and the vena cava may become more acute.

Exhaustive investigations of athletes who have presented with stress haematuria are often fruitless and neither site nor cause of the bleeding can be defined. The haematuria may be most difficult to induce deliberately so that clinical proof for the above suggested mechanism remains elusive.

Experimental animals such as rabbits and goats produce microscopic haematuria when subjected to high " g " forces. In a series of nine training pilots subjected to urine microscopy, five were found to have an increase in red cell excretion after " pulling 4·0 g. " for ten seconds, ten times each, during diving exercises.

Retrocaval Ureter

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The retrocaval ureter is a rare but interesting anomaly affecting the urinary tract. It is primarily a vascular anomaly resulting from abnormal development of the inferior vena cava; the ureter is secondarily involved. The condition was first reported in 1893; the total number of cases that have been reported is still small. The symptoms which present in this condition are usually due to dysfunction of the upper urinary tract, resulting from obstruction to the ureter in association with its retrocaval position. Recurrent urinary infection, renal pain, vague abdominal pain (especially in children) are common symptoms and may be associated with haematuria particularly if there is urinary tract infection.

The diagnosis is confirmed by the findings on excretory pyelography and inferior vena-cavography.

Surgical treatment is usually required and nephrectomy may be indicated in those patients in which the kidney is severely damaged by infection or hydronephrotic atrophy.

Conservative surgery may be accomplished by modified pyeloplasty but it is important to excise the portion of retrocaval ureter.

Division of the inferior vena cava with ligation of the upper and lower portions or reanastomosis of the cut ends, has been used in the treatment of this condition but would appear to be rather extensive and perhaps disturbing exercises in radical surgery to achieve an end result which can be more easily achieved by uretero-pelvic anastomosis after excision of the stenosed segment of the ureter.

Three patients with retrocaval ureter presented at the age of 66, 26 years and 7 years. The oldest patient presented with hypertension and refused surgical treatment of his anomaly. The youngest person was a boy with recurrent abdominal pain and urinary tract infection; he has made satisfactory progress following excision of the retrocaval ureteric segment with uretero-ureterostomy. The third patient, who was female, presented with right renal pain. Dilatation of the collecting system was relieved by Anderson-Hynes operation with excision of the retrocaval segment.

Intravenous Pyelography in Asymptomatic Cryptorchid Males

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Several autopsy series and several clinical studies have previously indicated a varying percentage of upper urinary tract anomalies to be associated with cryptorchidism. In Christchurch 135 patients, who were asymptomatic at the time of orchidopexy for cryptorchid or ectopic testes, were asked to undergo intravenous pyelography.

The results of the first 100 pyelographic studies revealed two major abnormalities and 12 minor abnormalities of the upper urinary tract.

The major abnormalities required surgical correction. One patient was found to have persistent gross bilateral vesico-ureteric reflux with bilateral loss of renal substance. A second patient was found to have bilateral complete pyelo-ureteric duplication with gross loss of renal substance in relation to reflux into the lower segment ureter of one kidney and with minor loss of renal substance in relation to the upper ureteric segment of the opposite kidney.

Abnormalities in the upper urinary tract were classified as minor if they were thought to be without clinical significance at the time of detection. Such abnormalities included three complete and one incomplete ureteric duplications. One patient showed persistent foetal lobulation, one had an ectopic kidney, one had a horse-shoe kidney without evidence of obstruction and one patient had Grade I congenital hydro-nephrosis which was asymptomatic with only a minimal degree of renal atrophy. Four other patients showed a non-obstructive type of ureteric dilatation in the lumbar or sacral segments, considered to be indicative of past or persistent vesico-ureteric reflux.

The incidence of 14% of upper urinary tract abnormalities in this series of patients undergoing orchidopexy is comparable to the incidence previously reported by other workers and is considered sufficient to justify a recommendation for the routine use of intravenous pyelography in all patients undergoing orchidopexy for cryptorchidism or ectopic testes.

Combined Therapy for Infiltrating Bladder Carcinoma

By J. H. DeWeerd, M.D.

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One hundred and eighty-six patients with infiltrating bladder cancer have been entered in a planned protocol which combines preliminary irradiation and surgical excision of the diseased tissue. Forty-three cases have been added to this ongoing study since the last summary report 18 months ago.

Only those patients whose age or other health problems preclude a vigorous therapeutic effort and those with massive, obviously inoperable, local disease or evident metastasis were excluded. No consideration has been given to random selection of patients in a homogenous atmosphere of a single institution.

One hundred and seventy-five patients completed the protocol. One hundred and forty-five of these were given a split-dose course of radiotherapy averaging 4,800 rads. Thirty had short concentrated three-day courses averaging a total of 2,400 rads. initially, but more recently averaging 1,800 rads. Total cystectomy, pelvic lymphadenectomy and urinary diversion were accomplished in 152 and partial cystectomy and pelvic lymphadenectomy in 17 patients. Inoperable lesions were found in six patients and operation was terminated after biopsy and urinary diversion in three instances.

Pathologic staging of lesions was combined with histopathologic grading to reveal that while most of the malignancies were stage B_1 or B_2, the numerical advantage over stages C and D was small. Approximately 80% were grade III or IV (Broders' classification). Forty-seven cases had no recognised residual intact carcinoma cells.

Operative mortality was low (3·4%) and morbidity and complications were in keeping with the magnitude of the surgical effort.

Survival of 23 patients (51% of 45) at risk for five to eight years and of 69 patients (57% of 122) at risk for two years suggests that when larger numbers can be adjusted by actuarial depletion, percentage survival may be in the range of 55% to 65%.

The utilisation of two distinctly different modalities, each effecting its own benefit in tandem in a planned protocol, continues to hold promise of increased chance of survival for the patient with invasive bladder cancer.

Pathogenesis and Management of Prostatitis

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Observations have been made of the leucocyte content and the bacterial population of the prostatic urethra in 50 male patients with clinical signs or symptoms of non-acute prostatic inflammation and in 15 control subjects without clinical suggestion of prostatic disease.

The leucocyte count in the initial urine samples before prostatic massage was usually less than 10 per ml. in both the patient and the control subjects. Prostatic massage produced a shift to more than 50 cells per ml. in 12 of the patients, but in only one of the control subjects.

In nine patients and two control subjects, the initial urines before and after massage were sterile, whilst in the remainder the distribution of organisms was almost identical between the clinical and the control groups. *Staphylococcus albus* was the commonest organism in both patients and controls (54% and 50%) with *Streptococcus faecalis* (20% and 25%), *Streptococcus viridans* (8% and 15%) and *Esch. coli* (11% and 10%) occurring less frequently in combined or pure culture. In only one specimen from any control subject were the viable counts in excess of 100 organisms per ml. The majority of the viable counts in both patients and controls were less than 100 organisms per ml. and prostatic massage did not change the incidence of organisms of different types in the initial urine, and only occasionally produced a marked change in the viable count.

Drug therapy reduced the bacterial counts without sterilisation of the posterior urethra.

In 40 patients operative treatment comprised instrumental over-stretch of the prostatic urethra with vigorous prostatic massage under general anaesthesia. Sixty-six per cent of the specimens of prostatic secretion thus obtained were sterile. This lowered incidence of bacterial content of prostatic secretion compared with initial urine samples could not be clearly attributed to pre-operative drug therapy or antiseptic contamination at cystoscopy.

These studies failed to define any bacterial population in the posterior urethra, which is specific to patients with so-called chronic prostatitis. No evidence was obtained that common "commensal" organisms such as *Staphylococcus albus*, *Streptococcus faecalis* and *Streptococcus viridans* are pathogenic in prostatitis. Retention of pathogenic organisms within the prostate could not be implicated as a source of recurrence or relapse of clinical prostatitis in this series. The basis for clinical improvement after chemotherapy, antibiosis or urethral instrumentation remains obscure.

These studies were carried out in collaboration with Associate Professor Douglas Smith and Dr R. H. Farnsworth with financial assistance from the Australian Kidney Foundation.

Further Thoughts on Prostatitis

By H. M. Learoyd, F.R.C.S., F.R.C.S.(Ed.), F.R.A.C.S.

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Chronic prostatitis is the commonest genito-urinary disease occurring in the male patient. The symptoms are variable and cover a wide spectrum of mental, emotional, urological and generalised physical illness.

Studies have been made to correlate changes in expressed prostatic secretions with varying degrees of prostatic infection—in most instances there is no correlation between the findings in the prostatic fluid and the clinical symptoms. Changes in size, contour and consistency of the prostate are usually coincidental.

The traditional method of treatment by "prostatic massage" appears to have no scientific basis to justify its continued use. The psychological aspects of the disease are usually overlooked and the doctor fails to appreciate that in most instances, he is dealing with an emotional illness.

Urodynamic Evaluation of Lower Urinary Tract Dysfunction

By C. U. McRae, F.R.C.S.
G. D. Chisholm, Ch.M., F.R.C.S.

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Consideration of dynamic aspects of the lower urinary tract should lead to better evaluation of patients presenting with lower urinary tract symptoms than can be obtained by mere consideration of any structural changes demonstrated by conventional methods of investigation. It is important that the urethral component of urodynamic evaluation be included and it has been found that examination of the urethral pressure profile may give additional valuable information.

Urodynamic assessment has been carried out on each of 50 patients whose symptoms were not readily explained by the results of conventional urological investigation. In each of these patients measurement of urine flow rate, bladder and rectal pressures during filling and emptying, together with urethral pressure profile, were all accomplished at a single investigation session. The findings indicated that most patients could be classified as having over-active detrusor, under-active detrusor, bladder outflow obstruction or reduced outflow resistance. The remaining patients' symptoms could not be explained on a urodynamic basis.

The Isolated Renal Pyramidal Infarct: Its Relationship to Calyceal Diverticulum and Pseudodiverticulum

By P. Julian Metzner, F.R.C.S.(Ed.), F.R.C.S., F.R.A.C.S.

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A group of 24 patients, with positive radiological evidence of calyceal diverticulum and pseudodiverticulum, have been studied with regards to clinical presentation, operative and pathological findings.

The average age at presentation was 29 years and the major presenting symptoms were recurrent urinary tract infection and recurrent or chronic loin pain.

Operative exposure of the kidney was carried out in 18 patients and in each of them tissue was obtained for pathological examination. Histological study showed that infarction of the renal medulla without evidence of chronic inflammation was common. Only three of the 18 patients did not have anomalous vascular supply to the involved kidney and aberrant arteries were noted in 11 of the patients. These pathological and anatomical features lead to the possible implication of isolated renal papillary infarction as the causal factor in the development of calyceal diverticulum and pseudodiverticulum. Such hypothesis takes into account the embryological development of renal vasculature and postulates that a single hypoxic episode during developmental life might account for the retention of mesonephric arteries and the incidental inclusion of intra-renal embryonal tissue in the definitive kidney.

Such mesonephric arteries would appear to lack the sophistication of normal vessels with regards to peripheral supply, so that areas in the renal medulla to which they are distributed might be more susceptible to stress to produce infarction and ultimately extra-calyceal cavity formation.

The Bladder Neck: A Theory of its Structure and Function

By D. J. Ellis, M.B., B.S., F.R.C.S.

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Reports relating to the anatomy and physiology of the bladder neck usually emphasise the role of smooth muscle fibres. This study was designed to assess the anatomy and role of striated muscle fibres in the mechanism of micturition.

Autopsy studies have been made of five normal neonates of whom three were female and two were male. In each subject the pelvis was prepared *en bloc* to include the pelvic organs and muscles, the symphysis pubis, sacral and coccygeal vertebrae and the inner periosteal lining of the pubic rami.

The specimens were fixed in formalin solution, blocked in paraffin and were cut in serial section in the sagittal plane before staining with haematoxylin and eosin and Masson stains to facilitate histological study of the arrangement of the smooth and voluntary muscle fibres.

The involuntary muscle of the urethra formed a heaped mass around the internal urethral orifice and was prolonged down to the perineal membrane as two thin longitudinal and circular muscle layers.

The voluntary muscle surrounded the involuntary muscle sleeve with its greatest concentration in the distal third of the posterior urethra—commonly referred to as the external sphincter zone. These fibres were circular in arrangement and could act as a sphincter. A significant but diminishing sleeve of circular-orientated striated muscle fibres, in continuity with the thicker muscle in the distal third, also extended proximally along the anterior and lateral and to a lesser extent along the posterior aspects of the urethra to within a few millimetres of the internal urethral orifice. In the male subject these fibres joined the fibro-muscular capsule of the prostate gland.

On the posterior aspect of the urethra, voluntary muscle fibres near the bladder neck were sparse in the male subject, whilst in the female subject definite striated fibres were recognised up to the region within a centimetre of the internal urethral orifice.

The outer sleeve of voluntary muscle was much greater in extent than is usually recognised. None of these fibres were arranged in a cranio-caudal direction or in a fashion which could tilt any muscular base-plate of the bladder. The puborectalis muscle was demarcated from these circular fibres and this muscle sling could be recognised skirting the distal third of the urethra on its way to and around the rectum. The puborectalis muscle could elevate and compress the urethra by concertina-like compression of the rectum and vagina and urethra towards the pubis.

The most cranial voluntary muscle fibres in the urethra appeared to be too sparse to create a sphincteric action. By analogy with the concepts of function of the voluntary muscle of the rectum, it could be argued that these fibres in the upper half of the urethra are chiefly proprioceptive and may create a stretch reflex and a warning mechanism of impending micturition.

The Technique of External Sphincterotomy

By W. H. Cadzow, M.B., B.S., F.R.C.S., F.R.A.C.S.

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In a personal series of 51 patients, three techniques of external sphincterotomy have been tried during the past six years.

1. *Colling's Knife Electrode with Panendoscope.*—This was the first method used. Deep lateral cuts were made from the verumontanum to the bulb of urethra at " three o'clock and nine o'clock ". This method was abandoned early in the series because manipulation of the panendoscope proved awkward and difficulty was experienced in coagulation of bleeding vessels in the depth of the linear cuts.

2. *Knife Electrode with Resectoscope.*—This technique was found to be much easier and more precise because of familiarity with the instrument but difficulty in visualisation of the linear cuts was again experienced.

3. *Standard Loop Electrode with Resectoscope.*—It was former practice to cut two lateral channels from the verumontanum down to the bulb of urethra but it was subsequently noted that a unilateral resection gave the same clinical benefit with significant less haemorrhage. The cut should be generous to the depth of the loop. Demonstration of residual muscle in the base of the resection is obtained by a contractility produced by stimulation with a coagulation current. Heavy bleeding often occurs especially if the corpus spongiosum is entered. Such venous bleeding tends to settle spontaneously when a urethral catheter is inserted and thus differs from the heavy venous bleeding encountered from the prostatic capsule during prostatic resection. A single cut with the standard loop electrode through the resectoscope has been adopted as the standard method of sphincterotomy.

Occasionally it is necessary to repeat the procedure once or twice before a satisfactory clinical result is obtained.

Endoscopic examination of the resected region at varying intervals after operation, showed that the cut channel persists as a rigid trough. It is thus possible that the inability of this scarred channel to be compressed by the remaining external sphincter is responsible for the decrease in outflow resistance in the urethra.

Management of the Paraplegic Bladder

By D. H. Keller, F.R.C.S., F.R.A.C.S.

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The management of the bladder in the paraplegic patient may be divided into four phases which relate to the stage of spinal shock, the return of bladder activity, the recovery of full bladder activity and the fourth phase of late complications.

During the phase of spinal shock, the aim of treatment is to prevent infection and over-distension of the bladder and this is accomplished by intermittent or continuous urethral catheter drainage.

During the phase of returning bladder activity, promotion of the upper motor neurone type of bladder function may be encouraged by stimulation of the bladder by suprapubic tapping, by straining and laughing, digital rectal stimulation, by pubic hair stimulation, or by cholinergic drugs. During this phase reduction of sphincter spasm may follow administration of Valium, Compound 34367 or may be induced by anaesthetic blockade of the pudendal or sacral nerves.

Compensated function in lower motor neurone bladder disorder may be promoted by Crede compression, straining and coughing, cholinergic drugs such as Ubretid or Carbachol and by patient posture training.

During the phase of full bladder activity, the ultimate aim is to achieve a satisfactory bladder state without catheter drainage; the bladder should empty two-hourly to leave a residual urine of less than 100 ml. and this should be relatively free of infection.

In the upper motor neurone type of bladder an unsatisfactory bladder state is usually due to spasm of the external urethral sphincter. This spasm may be relieved by pudendal neurectomy, sacral nerve rhizotomy, intrathecal alcohol injections and endoscopic resection of the external sphincter. In the absence of severe somatic spasms and significant autonomic hyper-reflexia division of the external sphincter is the treatment of choice.

In the lower motor neurone bladder pattern the problem is one of poor contraction of the detrusor muscle working against the sphincteric and urethral tone. Endoscopic resection of the bladder neck may be required to restore bladder balance but it may also be necessary to resect the external urethral sphincter.

Intermittent Catheterisation of the Paralysed Bladder

By E. J. England, F.R.C.S., F.R.C.S.(Ed.), F.R.A.C.S.
J.W. Pearman, M.B., B.S.,

Royal Perth Hospital, Perth, Western Australia

In a series of 36 patients who sustained acute traumatic paraplegia or tetraplegia, the urological management during the immediate and early period following spinal cord injury has been carried out by six-hourly intermittent urethral catheterisation, combined with the prophylactic urethral instillation of kanamycin and colistin.

Almost 80% of these patients had dispensed with the need for catheterisation within 60 days from the time of injury but eight patients required catheterisation for longer than 60 days. Two of these were tetraplegic females and two had lesions of the conus medullaris.

Approximately 80% of the patients developed adequate compensatory mechanisms of bladder emptying without requiring more than 200 catheterisations.

A total of 3,036 catheterisations were performed on the 27 male patients in the series with the occurrence of a total of 16 episodes of bacteriuria. The overall incidence of bacteriuria in catheterisation was 0·5% in male patients and 0·6% in female patients.

None of the 23 catheter-free male patients had significant bacteriuria at their discharge assessment. Of the nine female patients in the series, seven were discharged without significant bacteriuria but two patients with tetraplegia were discharged with indwelling urethral catheter draining and urinary tract infection.

This form of bladder management allowed for 30 of 33 surviving patients from the entire series to be discharged from hospital with residual urine of less than 80 ml. Two of the remaining patients were female tetraplegics with indwelling catheter drainage and one patient had had ileal conduit diversion.

Catheter Management of Spinal Injury Patients

By R. H. Farnsworth, F.R.C.S.(Ed.), F.R.A.C.S.

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The short-term results of management of patients with acute spinal cord injury by continuous bladder drainage with an indwelling urethral catheter have been studied in a group of 27 consecutive patients admitted to hospital over a period of three years.

At the time of discharge from hospital 84% of the patients were without catheters. The use of a sterile closed drainage system did not eliminate urinary infection during the period of catheter drainage. However, only one patient in the group without catheters showed definite bacteriological evidence of urinary infection during the period of follow-up.

There was a low incidence of bladder calculi and epididymitis and only one patient developed major urological complications necessitating suprapubic cystostomy. No patients in the group have developed radiological changes of pyelonephritis or renal calculus disease.

It is suggested that the indwelling urethral catheter still has a place in the early management of spinal injury patients and that progressive renal damage is unlikely unless chronic bacteriuria occurs in the presence of either vesico-ureteric reflux or obstructive uropathy.

Pathogenesis and Treatment of Calcium Stone Disease

By B. E. C. Nordin, M.D., Ph.D., F.R.C.P.

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(Visiting Professor: Australian Kidney Foundation)

Most calcium stones are composed of or contain calcium oxalate and calcium phosphate in varying proportions. A small proportion of idiopathic stones consist of almost pure calcium oxalate; pure calcium phosphate stones are generally secondary to hyperparathyroidism or renal tubular acidosis. The outstanding biochemical abnormality in the majority of these cases is a raised urinary calcium secondary to a high rate of calcium absorption. This increases the risk of over-saturation of the urine with calcium salts when the subjects are on normal or high calcium intakes. Precipitation of these salts corresponds to the saturation of the urine, and the logical treatment is to restrict calcium and oxalate intake, which is successful in most recurrent stone-formers.

In a minority of cases who form very frequent stones there is also evidence of reduced inhibitory activity in the urine, but such inhibitory activity does not appear to affect the precipitation of calcium salts but only the aggregation or growth of crystals and possibly the development of calcium oxalate dihydrate (as opposed to monohydrate) crystals.

Pathogenesis and Management of Uric Acid Calculi

By B. T. Emmerson, M.B., B.S., M.D., F.R.A.C.P.

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In the management of patients with uric acid calculi, it is most important to distinguish between those patients who are over-producers of urate and those who have normal urate production. In the group of over-producers, patients are characterised by a deficiency of an enzyme (hypoxanthine-guanine phosphoribosyltransferase), and the study of urate metabolism shows that renal excretory capacity is good but excretion of urate can equal production of urate. In such a situation the serum urate would be normal, whilst the level of urine uric acid would be elevated. At this stage such a patient would not suffer from gout but would be troubled chiefly by uric acid gravel and calculi. Such tendencies would promote uric acid cystal formation both in the renal tubules and in the renal pelvis and particularly at those times when the urine was highly concentrated or unduly acid in reaction. Eventually, some impairment of renal excretory capacity for urate will develop and will result in a gradual rise in the serum urate and a gradual reduction in urinary uric acid concentration. With the passage of time the increasing hyperuricaemia may lead to gout and microtophus formation in the kidney and the reduced renal exretory capacity may lead to sufficient lowering of the urinary uric acid whereby the tendency to calculus formation will subside. There is another group of patients who overproduce urate, who, from the onset, present with poor renal excretory capacity for urate and they become hyperuricaemic early in their clinical course and develop gout and tophi; in this particular group renal calculus formation is not a problem.

The second major group of patients with uric acid calculi have normal uric acid production. In this group, calculus formation is commonly associated with either excessive uric acid concentration in the urine or excessive urinary acidity. The concentration of other urinary constituents such as urea, sodium and calcium also plays an important role in modifying the tendency to uric acid calculus formation, so that a very high urine uric acid in the presence of a normal urine calcium may be associated with the formation of uric acid calculi, whereas in the presence of hyperuricosuria plus hypercalciuria any calculi formed tend to be composed of calcium oxalate.

From these considerations of uric acid calculus formation it could be concluded that those patients who are over-producers of urate should be treated with allopurinol to reduce urate production, whereas those who have normal urate production and who do not have excessive amounts of uric acid in their urine should be managed by persistent reduction of the uric acid concentration in their urine by regular consumption of fluid and alkalinisation of the urine.

Prevention of Recurring Kidney Stones

By K. J. Murphy, M.B., F.R.A.C.P.

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Investigation of patients with bilateral and recurrent kidney stones has included an oral ammonium chloride test to record hydrogen ion excretion by the measurement of urinary pH, urinary ammonium and urinary titratable acidity. In a group of 193 patients only 15 had a normal ammonium chloride test and no detectable cause of stone formation. In the absence of obvious and treatable causes, such as hyperparathyroidism, there was a high incidence of impaired excretion of hydrogen ion and, on the assumption that this was related to abnormal excretion or chelation of calcium, long-term treatment by the administration of potassium citrate has been tried.

Forty-seven patients on alkaline treatment have attended the clinic and taken regular medication for more then six months to provide a total patient experience of 217 years. During such surveillance, one patient has developed staghorn calculi on the basis of pre-existent renal papillary calcification; one patient has shown some enlargement of pre-existing renal stones but the other patients have either improved or failed to show any deterioration. Individual consideration of patients during follow-up periods of up to ten years has shown marked decrease in the rate of stone formation as the result of alkaline therapy.

The Blood Supply of the Kidney in Relation to the Surgery of Stone

By R. A. Syme, M.B., B.S., F.R.C.S., F.R.A.C.S.

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The arteries, veins and renal pelves of cadaver kidneys have been studied by resin injection and acid digestion, latex injection and formalin fixation and barium injection with radiology. Previous descriptions of the vascular anatomy of the kidney have been confirmed but the importance of the vascular anatomy in relation to pyelotomy, intrasinus pyelocalycotomy, nephrotomy and partial nephrectomy has been stressed.

The following points require particular emphasis:

(*a*) Division of any renal arterial vessel will result in infarction of the tissue supplied by that vessel, whereas division of a vein will not cause harm.

(*b*) Anarterial intersegmental planes do exist and form ideal sites for nephrotomy incisions; these planes can be found readily by temporary occlusion of the appropriate segmental artery when its area of supply will turn blue and soft. Incision along the margin of this area will not divide any significant artery and in combination with sinus dissection would allow for wide exposure of the calyceal system.

(*c*) Lateral renal resection would be logically performed by posterior segmental resection.

(*d*) Lower pole pyelocalycostomy endangers the posterior branch of the inferior segmental artery as it runs beneath the lower major infundibulum.

(*e*) Brodel's visually determined " bloodless plane " for longitudinal nephrotomy is dangerous and should be replaced by the intersegmental plane determined by arterial occlusion.

(*f*) Ligation of apparent polar vessels prior to partial nephrectomy is unsound, since the vascular segment does not closely correspond with the diseased calyces; moreover, the exact distribution of an apparent polar vessel cannot be visually determined without prior occlusion and it may supply segments of kidney which should be preserved.

Early Results in a Detailed Stone Analysis

By J. Stuart Taylor, F.R.C.S., F.R.A.C.S.

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Eight selected urinary calculi have been analysed using X-ray diffraction to determine the chemical compounds present. A search for the presence of significant trace elements was then undertaken with the use of optical emission spectrometry, X-ray fluorescence and atomic absorption spectroscopy.

Of the compounds, calcium oxalate monohydrate, calcium oxalate dihydrate, uric acid, struvite and hydroxyapatite were identified. In addition, a substance identified as cyanuric acid was found in the so-called uric acid stones. This substance has not been previously reported as a constituent of urinary calculi.

The nature and distribution of the compounds present were similar to those reported by other workers and calcium oxalate monohydrate was present in each calculus examined. When nuclei were present within the calculi, it was found that the composition of the nuclei differed from the rest of the stone; calcium oxalate monohydrate concentrated in the nuclei in these stones.

Arterial Injection as an Aid to Partial Nephrectomy

By J. L. Williams, M.B., B.S., F.R.C.S.

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Partial nephrectomy still carries a morbidity with secondary haemorrhage and fistula formation occurring in a varying proportion of cases. The segmental arterial anatomy of the kidney has been well described.

Injection of the appropriate segmental artery with an aqueous solution of 0·4% indigo carmine will accurately outline the part of the kidney which requires to be resected and, when this area has been removed, then no devascularised tissue is left behind. Secondary haemorrhage or persistent fistula formation have not occurred in the last 30 cases of partial nephrectomy in which this method has been used.

The Removal of Staghorn Calculi under Local Renal Hypothermia

By H. G. Hanley, M.D., F.R.C.S., F.A.C.S.(Hon.)

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Complete removal of all fragments of stone can only be achieved in the majority of patients by the use of contact X-ray during surgery, combined with thorough pelvic lavage in an avascular operative field, achieved by temporary arterial occlusion.

The safe limit of arterial occlusion in the kidney is about 15 minutes but this time may be insufficient for a thorough stone clearance.

The use of local renal hypothermia has enabled the surgeon to occlude the renal artery for periods in excess of one hour without demonstrable renal damage and time is thus allowed for several contact X-ray films to be exposed and for a complete clearance of stone to be accomplished.

Pyelo-venous Fistulae

By J. E. England, F.R.C.S., F.R.C.S.(Ed.), F.R.A.C.S.
A. Low, F.R.C.S., F.R.A.C.S.

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Renal bleeding due to small lesions of the renal papilla or fornix has been described under a variety of terms. The various pathological conditions occur infrequently and are difficult to delineate because of their size and position.

Three patients have presented with haematuria due to lesions of the renal fornix with a pathological basis upon veno-calyceal fistula.

Histopathological study of the renal fornices was carried out in 200 autopsies. The studies showed that only 13% of renal fornices were normal, whilst the remainder showed various histological abnormalities such as sub-epithelial cystic changes (30%) and fornical haemorrhages or iron-pigmented deposition (10%).

Any changes of the fornix, whether they be the effects of pressure, stasis, infection or hypoxia, are likely to lead to rupture of the unsupported walls of the venous sinuses and epithelium of the calyx with formation of veno-calyceal canals.

Demonstration of vascular channels which communicate with the calyceal cavity depends upon an awareness of these lesions and a planned method of examination of the kidney. Specimens of fresh kidney must be carefully hemisected and examined immediately after excision, because fixation of the fornix prevents adequate visualisation of the fornix without tearing of the papilla or the adjacent tissue of the wall of the calyx.

ABSTRACTS FROM CURRENT UROLOGICAL LITERATURE

Annals of Surgery

By J. E. A. Wickham

"Control of Hypercalcemia with Mithramycin." E. G. Elias, G. Reynoso, and A. Mittelman. (1972, **175,** 431-435.)—Administration of the antibiotic Mithramycin has been shown to reduce hypercalcaemia. 11 patients suffering from hypercalcaemia associated with malignant disease and 1 with parathyroid adenoma were studied. Effective reduction of the elevated serum calcium levels was produced in all patients with an alternate daily dosage of 25 μg./kg. of Mithramycin. No renal or bone marrow toxicity was experienced in this group. The mechanism of action of this drug is unknown.

"Effects of Renal Denervation and Renin Depletion on the Renal Responses to Intravascular Volume Expansion." L. L. Michaelis and J. P. Gilmore. (1972, **175,** 424-430.)—This paper describes a series of experiments designed to investigate the effect of denervation of the unanaesthetised dog's kidney with respect to subsequent handling of sodium and water. Dogs were studied pre- and post-denervation with water and saline loading. No statistical difference was found between the 2 groups of kidneys in their handling of salt and water, again confirming that the renal nerves have little if any importance in modulating natriuresis and diuresis following volume expansion. Pharmacological renin deprivation was also induced in the same animals by DOCA excess and salt administration and again demonstrated that renin was not required to induce the diuresis and natriuresis following intravascular volume expansion.

Acta Urologica Belgica

By Victor Lane

"Do Patients with Carcinoma of the Prostate Benefit from Oestrogen Treatment?" A. Coune. (1972, **40,** 97-100.)—In 1967 a co-operative study by 14 American departments of urology suggested that patients receiving a 5 mg. daily dose of diethylstilboestrol had a higher overall mortality than patients receiving no oestrogen, the increase in deaths mainly resulting from cardiovascular causes. A more recent study by the same group suggests that 1 mg. daily dose of diethylstilboestrol is effective in controlling cancer of the prostate without being associated with cardiovascular complications.

"Hormonal Treatment of Prostatic Cancer." L. Wemeau, E. Mazeman, J. Blanckaert and J. Delhay. (1972, **40,** 101-105.)—This survey reports the results of treating 168 cases of prostatic cancer by oestrogens during the period 1961 to 1965. 55% survived 2 years, 26% 5 years, and 15% 8 years.

"Long-lasting Results of the Hormonal Treatment for Prostatic Cancer." E. Ljunggren. (1972, **40,** 108-112.)—Ljunggren does not agree with the findings of the Veterans Administration Research Group (1967). He believes that oestrogen treatment (in the form of intramuscular Estradurin) should be started as soon as the diagnosis is made and a careful watch kept for any cardiovascular complications.

"Ectopic Implantation of the Ureter." Claude C. Shulman. (1972, **40,** 199-479.)—The entire issue is given over to a most extensive review of the embryology, investigation and treatment of the various varieties of this abnormality. The paper is superbly illustrated and contains a very full bibliography.

American Journal of Roentgenology

By B. H. Page

"Pelvic Lipomatosis." L. B. Morettin and McM. Wilson. (1971, **113,** 181-184.)—This is a report by 2 radiologists from Galveston, Texas, of a single case of a rare condition, only 11 cases having been reported in the English literature. An excessive deposition of fibro-adipose tissue in the pelvis compresses and elongates the rectum and bladder and produces a characteristic translucency in the X-ray film. The cystogram shows the bladder elongated vertically with a tapering base, the so-called inverted tear drop. The distortion of the organs does not affect their functions, the X-rays revealing the lipomatosis may be taken because of urinary symptoms just due to common pathological conditions such as prostatitis.

The Australian and New Zealand Journal of Surgery

By H. H. Pearson

"Urinary Infection and Catheterisation: A Case for a Catheter Team." W. M. Castleden. (1971, **41,** 65-68.)—A summary of 84 patients undergoing urethral catheterisation at the Royal Hospital, Western Australia, between December 1969 and August 1970 revealed that 45 (53·6%) developed significant bacteriuria. All patients had sterile urines before catheterisation. The author classifies the types of catheterisation as continuous and intermittent and shows that the infection rate increases in both sexes with the duration of catheterisation. The greatest infection rate occurred in elderly patients with retention following operations. Of the 39 patients who did not develop catheter infection 25 were being treated with antibiotics for their surgical or orthopaedic conditions. He concludes that these provide significant prophylaxis against the development of catheter bacteriuria. The literature in relation to attempts to reduce the infection rate is reviewed together with techniques of catheterisation and drainage. The author comments on the excellent results achieved by Pearman and England from the Spinal Injuries Unit at the Royal Perth Rehabilitation Hospital where, by a special technique of intermittent catheterisation, infection in quadriplegics and paraplegics is a rarity. He advocates the use of a catheter team within a hospital in an attempt to achieve similar results.

"Results of Surgical Treatment of Carcinoma of the

Penis." J. T. Kuruvilla, F. H. Garlick and K. E. Mammen. (1971, **41**, 157-159.)—The authors from the Department of Surgery, Christian Medical College and Hospital, Vellore, South India, report on a 5-year follow up of 153 patients treated surgically for carcinoma of the penis which accounts for 2% of all malignant tumours seen at this hospital. All patients were Indian and the majority a decade younger than those reported in Western series. They point out that it spreads by local infiltration and by lymphatics and that bloodstream spread is very rare. Their figures showed that Muslims who undergo childhood circumcision have 80% less chance of developing carcinoma than Hindus who do not undergo circumcision. Of the 153 patients at 5-year follow-up, 69 (45%) had died and 84 (55%) were known to be alive. 24 were not traced. Operative mortality was 1% and overall 5-year survival 55%. Treatment was by partial or total amputation with or without bilateral inguinal block dissection. Survival rates with the 3 techniques of operation are discussed, together with the correlation of clinico-pathological spread and the degree of differentiation. Local complications were recurrence, urethral stenosis, delayed wound healing and lymphoedema.

" Urinary Retention Due to Asymptomatic Protruded Lumbar Disc: Report of a Case." C. D. Vermillion, W. L. F. Utley and W. A. Liddell (1971, **41**, 182-184.)—Emmett and Love described their first case of urinary retention caused by a protruded lumbar disc in 1967. They have since seen and treated 35 other patients with similar findings. This latest figure includes several patients with symptoms typical of ruptured lumbar disc. The authors, from the Christchurch Hospital, Christchurch, New Zealand, report the case of a 33-year-old woman with urinary retention. Subsequent evaluation revealed an asymptomatic central protrusion of her L4-5 disc. This was removed and a spinal fusion carried out with relief of her symptoms. A cystometrogram 6 months after operation revealed sensation of filling at 400 ml. and extreme discomfort at 700 ml. There was less than 5 ml. of residual urine after voiding. The authors point out that myelographic findings may be equivocal and in many reported cases there has been a lack of neurological findings; Emmett and Love have largely relied on the characteristic history and cystoscopic findings in making their pre-operative diagnosis. Chronic constipation is a common concomitant finding.

Deutsche Medizinische Wochenschrift

By John Grieve

" Cortisone Cataract after Renal Transplantation." J. Mahlich, G. Thiel, D. Dobrinovojevic, F. Brunner and F. Enderlin. (1972, **97**, 860-865.)—Of 13 patients who had a renal allotransplant 10 developed cataract of varying severity. There were 2 main varieties of cataract, one of early onset and rapid development, the other not appearing till at least a year after transplant and progressing very slowly. The authors were able to relate the onset and severity of the cataract to the dosage of prednisone and its duration. In those with early severe cataract the prednisone dose was much higher than in the others and those over 40 years of age ran a much higher risk of developing cataract.

The Journal of the American Medical Association

By D. T. H Paine

" Cooperative Study of Renovascular Hypertension." Prepared by M. H. Maxwell, K. H. Bleifer, S. S. Franklin and P. D. Varady with the assistance of Claire Deegan. (1972, **220**, 1195-2131.)—This issue devotes all of its section for " original contributions " to this study. 15 medical institutions throughout the United States were participants. The methodology, organisation and demographic data are first set out. 2,442 patients were studied of which 1,128 had essential hypertension, 880 renovascular disease, 355 parenchymal kidney disease and 79 miscellaneous disorders There were 577 operations on 502 patients with renal artery disease. Of these, 384 were followed up at least 1 year.

" Clinical Characteristics of Renovascular Hypertension." N. Simon, S. S. Franklin, K. H. Bleifer and M. H. Maxwell.—These were reported from the North Western University-McGaw Medical Centre, Chicago, and the Department of Medicine, U.C.L.A. and the Cedars-Sinai Medical Centre, Los Angeles. They compare 175 patients with renovascular hypertension cured by surgery with 339 with essential hypertension. Features assessed included pain, bruit, age, sex, race, duration, family history, symptoms, general arterial disease and many other findings and pathology tests.

" The Radiological Aspects of Renovascular Hypertension." J. J. Bookstein, H. L. Abrams, R. E. Buenger, J. Lecky, S. S. Franklin, M. D. Reiss, K. H. Bleifer, E. C. Klatte and H. Maxwell.—The radiographic aspects were covered at several centres and concerned all aspects of technique and interpretation of the I.V.P. and the arteriogram. The major features included kidney length, calyceal appearance time, and concentration of contrast medium as well as ureteral notching, kidney width, radiographic density, etc. An effort was made to correlate urographic and arteriographic findings with therapeutic results to determine the reliability of the urogram as a screening procedure for unilateral renovascular disease and its usefulness in predicting surgical results. Major features were: disparity in renal length, calyceal appearance time and concentration on late films. Delayed appearance time seemed to be the single most valuable feature and it was concluded that urography is a satisfactory method for diagnosing the presence or absence of severe renovascular disease. Urography alone did not enable discrimination between those who would respond to surgery favourably and those who would not. A difference in renal length was considered to be significant if the left kidney was more than 1·5 cm. shorter or more than 2·0 cm. longer than the right. This co-operative study is very thorough and detailed and merits examination of the complete publication.

La Nouvelle Presse Medicale

By John Grieve

"Renal Transplantation between Donors and Recipients of Compatible HL-A Groups." J. Dausset and J. Hors. (1972, **1**, 1273-1279.)—The Transplant Association of France has collated the results of 426 kidney grafts between donors and recipients of compatible HL-A groups. The results confirm the major role played by the HL-A chromosome area on the fate of the graft and confirm the significant difference between the fate of grafts between cousins genetically identical for the HL-A system and other cousins ($p = < 0{\cdot}01$). HL-A incompatibilities definitely influence the prognosis for grafts between unrelated subjects. The percentage survival of the graft at 1 year was 68% in the most and 45% in the least compatible groups ($p = < 0{\cdot}001$). 2 years later the figures were 68% and 33%.

"**Second Renal Transplantations.**" M. Leski, H. Kreis, J. Auvert, M. Lacombe, J. Cukier and J. Crosnier. (1972, **1**, 1287-1290)—At the Necker Hospital, Paris, 214 renal transplants were carried out with cadaver kidneys on 200 patients. A study of the 14 second transplants and comparison with first transplants showed the following:—1. Very acute rejection (cortical necrosis) was the most frequent cause of failure in second transplants. 2. The overall results of second transplants were similar to those of first. 3. The functional results assessed on the clearance of endogenous creatinine after 6 months and 2 years were similar in both groups.

Surgery, Gynaecology and Obstetrics

By Thomas Moore

"**Simple and Ectopic Ureterocele in Infancy and Childhood.**" R. S. Malek, P. P. Kelalis, E. C. Burke, and G. B. Stickler. (1972, **134**, 611-616.)—In the 35 years between 1935 and 1969, 40 children with ureteroceles were encountered in the Departments of Urology and Pediatrics of the Mayo Graduate School of Medicine, University of Minnesota, Rochester. 33 were girls and 7 were boys, varying in age from 2 weeks to 15 years, with an average age of 4·8 years. The ureterocele was intravesical in 26 cases and ectopic in 14. The condition was 1·3 times more common on the right side. A few patients responded satisfactorily to prolonged follow-up on chemotherapy or transurethral incision of the ureterocele. Most required excision of the abnormal ureter and its feeding kidney segment. Cure was eventually obtained in all patients, in a follow-up period between 1 and 27 years.

"**Ureteral Implantation in Renal Transplantation.**" E. Anderson, J. F. Glenn, H. F. Seigler, and D. L. Stickel. (1972, **134**, 494-496.)—From the Division of Urology, Duke University Medical Centre, Durham, North Carolina, the authors describe their techniques for implanting the ureter of a transplanted kidney. The method is fairly orthodox, employing a submucosal tunnel. Of 81 patients 8 had ureteral complications: in 5 ureteral obstruction followed, 2 developed ureteric fistulae and in 1 a temporary vesical leak occurred.

"**Experience in Human Renal Allotransplantation.**" J. E. Woods, J. H. DeWeerd, W. J. Johnson, C. F. Anderson and R. G. Shorter. (1972, **134**, 394-398.)—From the Mayo Clinic and Mayo Foundation, Rochester, Minnesota, the authors report their results in 56 renal allografts in 53 patients with a minimum follow-up of 2 years. With related living donors the patients' 2-year survival rate was 87%; it was 67% in cadaveric donor kidneys. The kidney survival rates for the 2 groups were 80% and 33% respectively. Those with kidneys from living related donors had better kidney function, both early and late, required less dialysis, less immunosuppression therapy and suffered fewer complications. In the series the commonest causes of death were sepsis and intestinal haemorrhage. Wound infection and urological complications were rare. No urinary leaks or fistulae occurred. No indwelling ureteral catheter was used, only a urethral catheter for 10 days.

Der Urologe

By John Grieve

"**Infra-Red Thermometry in the Differential Diagnosis of Testicular Swellings.**" H. Rudolph, K. Hochberg, D. Bokelmann and G. Lepper. (1972, **11**, 77-79.)—Scrotal skin temperature was measured with an infra-red thermometer in 70 normals and 74 patients with testicular disease. In acute epididymitis and malignant tumours the affected side showed a rise of 1·2° and 1·4°C respectively. In varicoceles and chronic infections the rise was approximately a half of these figures and in hydrocele the temperature was almost a degree lower than normal. The authors from Heidelberg suggest that these changes can be simply observed and are helpful in differential diagnosis.

"**The Clinical Significance of the Measurement of Absorption of Irrigating Fluids during Transurethral Resection of the Prostate.**" K. Naber, H. Kuni, H. Sommerkamp and K. H. Bichler. (1971, **10**, 261-265.)—The intravascular absorption of irrigating fluid (5% glucose) was measured during prostatic resection using ^{131}I labelled albumen. A scintillation detector placed over the lungs monitored the absorption of the labelled albumen throughout the operation. At the end of the operation the paravascular absorption of the labelled indicator in the bladder area was measured by another scintillation detector placed over the bladder. Two types of absorption occurred—sudden and continuous. Sudden absorption was more often observed when a large gland was resected and was considerable in amount. There was good correlation between the rise in blood sugar and the amount of irrigating fluid absorbed.

"**In Vitro Investigations on the Etiology of Bladder Carcinoma.**" K. Hochberg, L. Rohl and W. Kochen. (1972, **11**, 98-102.)—This study from Heidelberg was aimed at examining by tissue culture techniques the role of tryptophan metabolites and in particular 2 hydroxy-anthranilic acid in bladder cancer. Explants were obtained from 11 bladder cancers. In 312 of the cultures lysin ethyl ester was added and 217 of these showed epithelial growth. In 242 cultures to which no lysin ethyl ester was added only fibroblasts grew. A further experiment involved the uptake of labelled 2-hydroxy-anthranilic acid by tumour cells. This was demonstrated by autoradiography. The authors believe that the tissue culture technique is of value in the study of tryptophane metabolism.

"**Avascular Renal Tumours: the Clinical and Histological Features.**" B. Riedel, H. Baumgärtel, D. Bachmann and S. Grohme. (1972, **11**, 60-64.)—In a series of 56 renal tumours 8 showed as an avascular space-occupying lesion, the initial diagnosis being a cyst. At operation 6 proved to be tubulo-papillary carcinomas, 1 an adenoma and 1 a metastasis from a bronchial carcinoma. The authors conclude that operation is desirable in all cases diagnosed as solitary cysts because of the risk of carcinoma being diagnosed as a cyst and the fact that about 5% of cysts show carcinoma in the wall.

Zeitschrift fur Urologie

By JOHN GRIEVE

"The Differential Diagnostic Value of an Enzyme Pattern in Urine." R. HAUTMANN, A. SCHIFFER, S. LYMBEROPOULAS and W. LUTZEYER. (1972, 65, 533-543.)—In a series of experiments in guinea-pigs this Aachen group found that in:—(*a*) *Hypoxia*—urinary GOT (Glutamic oxalacetate transaminase) increased relative to urinary GPT (Glutamic pyruvate transaminase). (*b*) *Poisoning*—urinary alkaline phosphatase exceeded leucine aminopeptidase. (*c*) *Pyelonephritis*—urinary lactic dehydrogenase was greater than urinary malic dehydrogenase. These findings suggested to the authors that there may be similar patterns in human disease.

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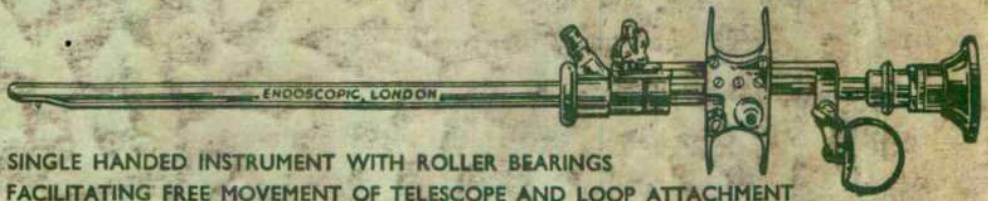
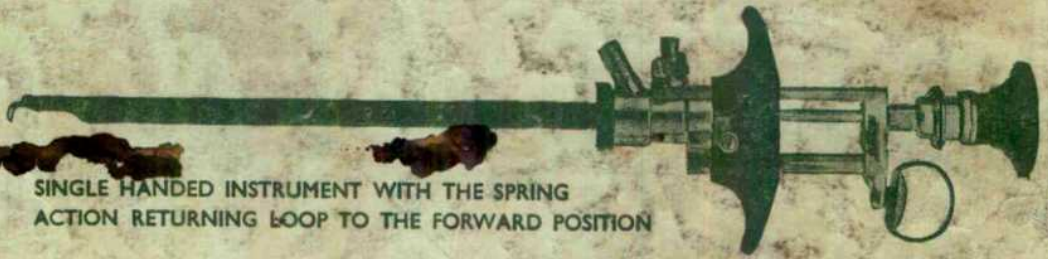


SINGLE HANDED INSTRUMENT WITH ROLLER BEARINGS
FACILITATING FREE MOVEMENT OF TELESCOPE AND LOOP ATTACHMENT

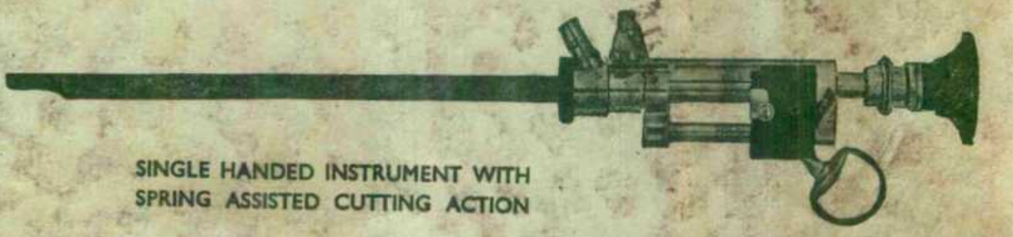
Developed for Mr J. P. MITCHELL, F.R.C.S., Bristol

BAUMRUCKER



SINGLE HANDED INSTRUMENT WITH THE SPRING
ACTION RETURNING LOOP TO THE FORWARD POSITION

NESBIT



SINGLE HANDED INSTRUMENT WITH
SPRING ASSISTED CUTTING ACTION

ENDOSCOPIC INSTRUMENT COMPANY LTD.
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